USE IN THE ELDERLY
In clinical studies., there were no clinicaly significant differences in the efficacy and safety profiles of Diu-Tansin in order (≥65 years) and younger parients (<65 years)

DRUG INTERACTIONS
Losartan:
In clinical pharmacokinetic trials, no drug-interactions of clinical significance have been indentified with hydrochlorothiazide,digoxin, warfarin, cimetidine, phenobarbetal, ketoconalzole and eryhromycin. Rifampin and fluconazole have been reported to reduce levels of active metabolite. The clinical consequences of these interactions have been evaliated.

As with other drugs that block angiotensin II or its effects, concomitant use of potassium sparing diuretics (e.g.,Spironolactone, triamterance, amiloride) potassium supplements, or salt substitutes containing potassium may lead to increase in serum potassium.

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

Hydrocholothiazide:
When given concurrently, the following drugs may intratc with thiazide diuretics:
Alcohal, barbiturates, or narcotics - potentation of othostatics hypertension may accur.
Antidiabetic drugs (oral agents and insulin) - dosage adjustment of the antidiabetic drug may be required.
Other antihypertensive drugs - additive effect.
Cholestyrarnine and colestipol resins - Single doses of either cholestyrarnine 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 prectude 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 ahigh risk of lithium. toxicity; concomitant use is not recommmended.
Non Steroidal Anti-inflammatory Drugs - in some patients, the admistration of a, non-steroidal anti-inflammatory agent can reduce the diuretics, natriuretic, and antihypertensive effects of diuretics.

Drug/Laboratory Test Interactions
Because of their effects on calcium metabolism, thiazide may interfare with tests for parathyroid fuction (see PRECAUTIONS).

SIDE EFFECTS
In clinicla trials with losartan potassium-hydrochlorothizide, 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 comparable to placebo. The percentage of discintinations of therapy was also comparable to placebo.

In general, treatment with losartan potassium-hydrochlorothiazide was well toleratec. 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 accured 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:

Hypersensivity: Anaphylactic reactions, including swelling of the larynx and glottis causing airway obstruction and/or swelling of the face, lips, pharynx and or tongue be reported rarely in patient with losartan; some of these patients previously experienced angioedema with other drugs including ACE inhibilators. Vasculities, including Henoch-Schoenlein purpura, has been reported rarely with losartan.
Gasterointestinal: Hepatitus has been reported rarely in patient treated with losartan, diarrhea.
Respiratory: Cough has been reported with losartan.
Skin: Urticaria.

Laboratory Test Findings
In controlled clinical trials, clinically important changes in standard laboratory parameters were rarely associated with administration of Diu-Tansin. Hypercalemia (serum potassium >5.5 mEq/L) accued in 0.7% of patients, but in these trials, discontinuation of Diu-Tansin due to hyperkalemia was not necessary. Elevations of ALT accured rarely and usually resolved upon discontinuation of therapy.

OVERDOSAGE
No specific information is availble on the treatment of overdosage with Diu-Tansin, Treatment is symptomatic and supportive. Therapy with Diu-Tansin should be discontiued and the patient observed closely, Suggested measure include induction of emesis if ingestion is recent, and correction of dehydration, electriolyte imbalance, hepatic coma and hypotension by established procedures.

Losartan
Limited data are avaiable in regard to overdosage in humans. The most likely manifestation of overdosage would be hypotension and tachycardia; bradycardia could accur from parasympathetic (vagal) sitimulaton. If symptomatic hypotension should accur, 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 by electrolyte depletion (hypokalemia, hydrochloremia, hyponatremia) and dehydration resulting from excessive diuresis. If digital has also been admisnistered, hypokalemia may accentuate cardiac arrhythmias. The degree to which hydrochlorothiazide isremoved by hemidialysis has not been established.

PRESENTATION
Diu-Tensin : Box of 10 film-coated tablets packed in blister.

Dosage & Instructions:
As advised by the physician.
Keep all medicines out of the reach of children.
To be sold on the prescription of a registered medical practitioner only.
Protect from heat, light and moisture.
Store below 30°C.

خوراک و ہدایات:
ڈاکٹر کی ہدایات کے مطابق استعمال کریں۔
تمام دوائیں بچّوں کی پہنچ سے دُور رکھیں۔
صرف رجسٹرڈ ڈاکٹر کے نسخہ پر ہی فروخت کی جائے۔
روشنی، گرمی اور نمی سے محفوظ، 30°C سے کم درجہ حرارت پر رکھیں۔

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RV : 01 04/2015

Diu-Tansin®

ڈائی یُوٹین سِن

(Losartan potassium and Hydrochlorothiazide USP)

COMPOSITION
Each film coated tablet contains:
Losartan potassium USP.....50 mg
Hydrochlorothiazide USP.....12.5 mg
(USP Specs.)

THERAPEUTIC CLASS
Diu-Tansin Losartan potassium and hydrochlorothiazide is the first combination of an angiotensin II receptor(type AT_1) antagonist and 1 diuretic.

INDICATION
Diu-Tansin is indicated for the treartment of hypertension, for patients in whom combination therapy is appropriate.

DOSAGE AND ADMINISTRATION
The usual starting and maintenance dose of Diu-Tansin is tablet(losartan potassium50 mg/hydrochlorothiazide 12.5mg) once daily. For patients who not respond adequately to Diu-Tansin, the dosage may be increased to two tablets of Diu-Tansin once saily. The maximum dose is two tablets of diu-tansin once daily. In general the antithypertensive effect is attained within three weeks after initiation of therapy.
Diu-Tansin should not be intiated in patients who are intravascularly volume depleted (e.g., those treated with high-dose diuretics).
Diu-Tansin is not recommended for patients with severe renal impairment (creatinine clearance ≤30 mL/min) or for patients with hepatic impairment.

No intial dosage adjustment of Diu-Tansin is necessary for elderly patients.
Diu-Tansin may be administered with other antihypertensive agents.
Diu-Tansin may be administered with or without food.

CONTRAINDICTIONS
Diu-Tensin is contraindicated in patients:
- who are hypersensitive to any component of this product.
-with anuria.
- who are hypersensitive to other sulfonamide-derived drugs.

PRECAUTIONS
Losartan-Hydrochlorothiazide
Hypersensitivity: Angioederna.
Hepatic and Renal Impairment: Diu-Tansin is not recommended for patients with hepatic impairment or severe renal impairment (creatinie clearance ≤30 ml/min).

Losartan
Renal Function Impairment: 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 increase serum creatinne 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, symtomatic hypotension - may occure in some patients Pateints should be observed for clinical signs of fluid or electrolyte imbalance, e.g. volume depletion, hyponatremia , hypochloremic alkalosis, hypomagnesemia or hypokalemia which may accur during intercurrent diarrhea of vomiiting. 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 antidiabetic 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 carring out tests for parathyroid fucntion.

Increase in cholestrol and triglyceride levels may be associated with thiazide diuretic therapy .

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

Other: in patients receiving thiazides, hypersensivity reactions may accure with or without a history of allergy or bronchial asthema. Exacerbation or activation of systemic lupus erythematosus has been reported with the use of thiazide.

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, Diu-Tensin should be discontinued as soon as possible.

Although there is no experience with the use of Diu-Tensin in pregnant women, animal studies with losartan postassium have demonstrated fetal and neonatal injury and death, mechanism of which is beleived to be pharmacologically mediated through effects on the renin-angiotensin system. In humans, fetal renal perfusion, which is dependent upon the development of the renin-angiotensins system, begins is in 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 to fetus unnecassary hazard including fetal or neonatal jaundice, thrombocytopenia and other adverse reaction which have accured 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 important of the drug to the mother.

PEDIATRIC USE
Safety and effectiveness in children have not been established.