SUMMARY OF PRODUCT CHARACTERISTICS

SARANTO–H 50 mg/12.5 mg TABLETS

(Losartan Potassium and Hydrochlorothiazide Tablets 50 mg/12.5 mg)

R_x Only

1. NAME OF THE DRUG PRODUCT: **SARANTO–H 50 mg/12.5 mg TABLETS** (Losartan Potassium and Hydrochlorothiazide Tablets 50 mg/12.5 mg)

2. NAME AND STRENGTH OF ACTIVE INGREDIENT: Losartan Potassium Ph.Eur. 50 mg and Hydrochlorothiazide Ph.Eur. 12.5 mg

3. DOSAGE FORM: Film-Coated Tablet

4. PRODUCT DESCRIPTION:

Yellow colored, oval shaped, beveled edge, biconvex film coated tablets debossed with ‘E’ on one side ‘48’ on the other side.

5. Pharmacodynamics/Pharmacokinetics:

5.1 Pharmacodynamics
Pharmacotherapeutic group: Angiotensin II antagonists and diuretics

Losartan -Hydrochlorothiazide

The components of Losartan and Hydrochlorothiazide have been shown to have an additive effect on blood pressure reduction, reducing blood pressure to a greater degree than either component alone. This effect is thought to be a result of the complimentary actions of both components. Further, as a result of its diuretic effect, hydrochlorothiazide increases plasma renin activity, increases aldosterone secretion, decreases serum potassium, and increases the levels of angiotensin II. Administration of Losartan blocks all the physiologically relevant actions of angiotensin II and through inhibition of aldosterone could tend to attenuate the potassium loss associated with the diuretic.

Losartan has been shown to have a mild and transient uricosuric effect. Hydrochlorothiazide has been shown to cause modest increase in uric acid; the combination of Losartan and hydrochlorothiazide tends to attenuate the diuretic induced hyperuricemia.

The anti hypertensive effect of Losartan Potassium and hydrochlorothiazide is sustained for 24-hour period. In clinical studies of one year duration, the antihypertensive effect was maintained with continued therapy .Despite the significant decrease in blood pressure, administration of Losartan Potassium and Hydrochlorothiazide had no significant effect on heart rate.

Losartan Potassium and Hydrochlorothiazide is effective in reducing blood pressure in males and females, blacks and non-blacks and in younger (<65 years) and older ($\geq$65 years) patients and is effective in all degrees of hypertension.

Losartan

Losartan is a synthetically produced oral angiotensin-II receptor (type AT_1) antagonist. Angiotensin II, a potent vasoconstrictor, is the primary active hormone of the renin-angiotensin system and an important determinant of the pathophysiology of hypertension. Angiotensin II binds to the AT_1 receptor found in many tissues (e.g. vascular smooth muscle, adrenal gland, kidneys and the heart) and elicits several important biological actions, including vasoconstriction and the release of aldosterone. Angiotensin II also stimulates smooth-muscle cell proliferation.

Losartan selectively blocks the AT_1 receptor. *In vitro* and *in vivo* Losartan and its pharmacologically active carboxylic acid metabolite E-3174 block all physiologically relevant actions of angiotensin II, regardless of the source or route of its synthesis.

Losartan does not have an agonist effect nor does it block other hormone receptors or ion channels important in cardiovascular regulation. Furthermore, Losartan does not inhibit ACE (kininase II), the enzyme that degrades bradykinin. Consequently, there is thus no increase in bradykinin-mediated undesirable effects.

During the administration of Losartan the removal of the angiotensin II negative feedback on renin secretion leads to increased plasma-renin activity (PRA). Increase in the PRA leads to an increase in angiotensin II in plasma. Despite these increases, antihypertensive activity and suppression of the plasma aldosterone concentration are maintained, indicating effective angiotensin II receptor blockade. After the discontinuation of Losartan, PRA and angiotensin II values fell within 3 days to the baseline values.

Both Losartan and its principal active metabolite have a far greater affinity for the AT_1 receptor than for the AT_2 receptor. The active metabolite is 10- to 40-times more active than Losartan on a weight for weight basis.

In a study specifically designed to assess the incidence of cough in patients treated with Losartan as compared to patients treated with ACE inhibitors, the incidence of cough reported by patients receiving Losartan Potassium or Hydrochlorothiazide was similar and was significantly less than in patients treated with an ACE inhibitor.

In nondiabetic hypertensive patients with proteinuria, the administration of Losartan potassium significantly reduces proteinuria, fractional excretion of albumin and IgG. Losartan maintains glomerular filtration rate and reduces filtration fraction. Generally Losartan causes a decrease in serum uric acid (usually <0.4 mg/dL) which was persistent in chronic therapy.

Losartan has no effect on autonomic reflexes and no sustained effect on plasma norepinephrine.

In patients with left ventricular failure, 25 mg and 50 mg doses of Losartan produced positive hemodynamic and neurohormonal effects characterized by an increase in cardiac index and decreases in pulmonary capillary wedge pressure, systemic vascular resistance, mean systemic arterial pressure and heart rate and a reduction in circulating levels of aldosterone and norepinephrine, respectively. The occurrence of hypotension was dose related in these heart failure patients.

Hypertension Studies

Discontinuation of Losartan in hypertensive patients did not result in an abrupt rise in blood pressure (rebound). Despite the marked decrease in blood pressure, Losartan had no clinically significant effects on heart rate.

Losartan is equally effective in males and females, and in younger (below the age of 65 years) and older hypertensive patients.

Hydrochlorothiazide

Hydrochlorothiazide is a thiazide diuretic. Thiazides affect the renal tubular mechanisms of electrolyte reabsorption, directly increasing excretion of sodium and chloride in approximately equivalent amounts.

The diuretic action of hydrochlorothiazide reduces plasma volume, increases plasma renin activity and increases aldosterone secretion, with consequent increases in urinary potassium and bicarbonate loss, and decreases in serum potassium. The renin-aldosterone link is mediated by angiotensin II and therefore coadministration of an angiotensin II receptor antagonist tends to reverse the potassium loss associated with thiazide diuretics.

After oral use, diuresis begins within 2 hours, peaks in about 4 hours and lasts about 6 to 12 hours the antihypertensive effect persists for up to 24 hours.

Non-melanoma skin cancer:

Based on available data from epidemiological studies, cumulative dose-dependent association between HCTZ and NMSC has been observed. One study included a population comprised of 71,533 cases of BCC and of 8,629 cases of SCC matched to 1,430,833 and 172,462 population controls, respectively. High HCTZ use (≥ 50,000 mg cumulative) was associated with an adjusted OR of 1.29 (95% CI: 1.23-1.35) for BCC and 3.98 (95% CI: 3.68-4.31) for SCC. A clear cumulative dose response relationship was observed for both BCC and SCC. Another study showed a possible association between lip cancer (SCC) and exposure to HCTZ: 633 cases of lip-cancer were matched with 63,067 population controls, using a risk-set sampling strategy. A cumulative dose-response relationship was demonstrated with an adjusted OR 2.1 (95% CI: 1.7-2.6) increasing to OR 3.9 (3.0-4.9) for high use (~25,000 mg) and OR 7.7 (5.7-10.5) for the highest cumulative dose (~100,000 mg).

5.2 Pharmacokinetics

Absorption

Losartan

Following oral administration, Losartan is well absorbed and undergoes first-pass metabolism, forming an active carboxylic acid metabolite and other inactive metabolites. The systemic bioavailability of Losartan tablets is approximately 33%. Mean peak concentrations of Losartan and its active metabolite are reached in 1 hour and in 3-4 hours, respectively. There was no clinically significant effect on the plasma concentration profile of Losartan when the drug was administered with a standardized meal.

Distribution

Losartan

Both Losartan and its active metabolite are $\geq$99% bound to plasma proteins, primarily albumin. The volume of distribution of Losartan is 34 liters.

Hydrochlorothiazide

Hydrochlorothiazide crosses the placental but not the blood-brain barrier and is excreted in breast milk.

Biotransformation

Losartan

About 14 % of an intravenously or orally-administered dose of Losartan is converted to its active metabolite. Following oral and intravenous administration of ^{14}C-labelled Losartan potassium, circulating plasma radioactivity primarily is attributed to Losartan and its active metabolite.

In addition to the active metabolite, inactive metabolites are formed, including two major metabolites formed by hydroxylation of the butyl side chain and a minor metabolite, an N2-tetrazole glucuronide.

Elimination

Losartan

Plasma clearance of Losartan and its active metabolite is about 600 mL/min and 50 mL/min, respectively.

Renal clearance of Losartan and its active metabolite is about 74 mL/min and 26 mL/min, respectively.

When Losartan is administered orally, about 4% of the dose is excreted unchanged in the urine, and about 6% of the dose is excreted in the urine as active metabolite. The pharmacokinetics of Losartan and its active metabolite are linear with oral Losartan potassium doses up to 200 mg.

Following oral administration, plasma concentrations of Losartan and its active metabolite decline polyexponentially with a terminal half-life of about 2 hours and 6-9 hours, respectively. During once-daily dosing with 100 mg, neither Losartan nor its active metabolite accumulates significantly in plasma.

Hydrochlorothiazide

Hydrochlorothiazide is not metabolized but is eliminated rapidly by the kidney. When plasma levels have been followed for at least 24 hours, the plasma half-life has been observed to vary between 5.6 and 14.8 hours. At least 61 percent of the oral dose is eliminated unchanged within 24 hours.

Characteristics in Patients

Losartan -Hydrochlorothiazide

The plasma concentrations of Losartan and its active metabolite and the absorption of hydrochlorothiazide in elderly hypertensives are not significantly different from those in young hypertensives.

Losartan

Following oral administration in patients with mild to moderate alcoholic cirrhosis of the liver, plasma concentrations of Losartan and its active metabolite were, respectively, 5-fold and 1.7-fold greater than those seen in young male volunteers.

Neither Losartan nor the active metabolite can be removed by hemodialysis.

6. Indication

Hypertension: Losartan Potassium and Hydrochlorothiazide Tablets is indicated for the treatment of hypertension, for patients in whom combination therapy is appropriate.

Hypertensive Patients with Left Ventricular Hypertrophy: Losartan Potassium and Hydrochlorothiazide Tablets is indicated to reduce the risk of stroke in patients with hypertension and left ventricular hypertrophy, but there is evidence that this benefit does not apply to Black patients.

7. Recommended Dose:

Losartan Potassium and Hydrochlorothiazide Tablets may be administered with other antihypertensive agents.

Losartan Potassium and Hydrochlorothiazide Tablets may be administered with or without food.

Fixed-dose combination is not indicated for initial therapy.

Hypertension: The usual starting and maintenance dose of Losartan Potassium and Hydrochlorothiazide Tablets is 1 tablet of Losartan Potassium and Hydrochlorothiazide Tablets 50/12.5 once daily. For patients who do not respond adequately to Losartan Potassium and Hydrochlorothiazide Tablets 50/12.5, the dosage may be increased to 2 tablets of Losartan Potassium and Hydrochlorothiazide Tablets 50/12.5 once daily. The maximum dose is 2 tablets of Losartan Potassium and Hydrochlorothiazide Tablets 50/12.5 once daily. In general, the antihypertensive effect is attained within 3 weeks after initiation of therapy.

Losartan Potassium and Hydrochlorothiazide Tablets should not be initiated in patients who are intravascularly volume-depleted (e.g., those treated with high-dose diuretics).

Losartan Potassium and Hydrochlorothiazide Tablets is not recommended for patients with severe renal impairment (creatinine clearance ≤30 mL/min) or for patients with hepatic impairment.

No initial dosage adjustment of Losartan Potassium and Hydrochlorothiazide Tablets is necessary for elderly patients.

Hypertensive Patients with Left Ventricular Hypertrophy: The usual starting dose is 50 mg of losartan once daily. If goal blood pressure is not reached with losartan 50 mg, therapy should be titrated using a combination of losartan and a low dose of hydrochlorothiazide (12.5 mg) and, if needed, the dose should then be increased to Losartan 100 mg and Hydrochlorothiazide 12.5 mg once daily. If necessary, the dose should be increased to Losartan 100 mg and hydrochlorothiazide 25 mg once daily.

7.1 Mode of Administration
Oral use.

8. Contraindication

Concomitant use of (active ingredient of ARB) with aliskiren-containing products is contraindicated in patients with diabetes mellitus or renal impairment (GFR < 60 ml/min/1.73 m2).

Losartan Potassium and Hydrochlorothiazide Tablets is contraindicated in patients who are hypersensitive to any component of this product, patients with anuria and patients who are hypersensitive to other sulfonamide-derived drugs.

Losartan Potassium and Hydrochlorothiazide Tablets should not be administered with aliskiren in patients with diabetes.

9. Warning and Precautions

Losartan-Hydrochlorothiazide:

Fetal Toxicity:

Use of drugs that act on the renin-angiotensin system during the second and third trimester of pregnancy reduces fetal renal function and increases fetal and neonatal morbidity and death. Resulting oligohydramnios can be associated with fetal lung hypoplasia and skeletal deformations. Potential neonatal adverse effects include skull hypoplasia, anuria, hypotension, renal failure, and death. When pregnancy is detected, discontinue Losartan Potassium and Hydrochlorothiazide Tablets as soon as possible.

Hypersensitivity:

Angioedema.
Hepatic and Renal Impairment: Losartan Potassium and Hydrochlorothiazide Tablets 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 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: these changes in renal function maybe 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 intercurrent 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 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 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.

Non-melanoma skin cancer

An increased risk of non-melanoma skin cancer (NMSC) [basal cell carcinoma (BCC) and squamous cell

A/s: 210 x 420 mm ■ Black Booklet Size: 35 x 60 mm

AUROBINDO Packaging Development		Product Name	Component	Item Code	Date & Time
		SARANTO–H 50 mg/12.5 mg	Leaflet	P1522342	26.12.2024 & 05.10 pm
		Country	Version No.	Reason Of Issue	Reviewed / Approved by
		Malaysia	08	Submission	
Team Leader	Kiran.k	Dimensions (mm)	No Of Colours: 01		
Initiator	Shirisha	A/s: 210 x 420 mm	22342		
Artist	Advnt (Rakesh)	Pharma Code: 22342			
Additional Information: WOS-19-000644		Supersede Code: P1514424			

carcinoma (SCC)] with increasing cumulative dose of hydrochlorothiazide (HCTZ) exposure has been observed in two epidemiological studies based on the Danish National Cancer Registry. Photosensitizing actions of HCTZ could act as a possible mechanism for NMSC.

Patients taking HCTZ should be informed for the risk of NMSC and advised to regularly check their skin for any new lesions and promptly report any suspicious skin lesions. Possible preventive measures such as limited exposure to sunlight and UV rays and, in case of exposure, adequate protection should be advised to the patients in order to minimize the risk of skin cancer. Suspicious skin lesions should be promptly examined potentially including histological examinations of biopsies. The use of HCTZ may also need to be reconsidered in patients who have experienced previous NMSC.

Acute Respiratory Toxicity: Very rare severe Cases of acute respiratory toxicity, including acute respiratory distress syndrome (ARDS) have been reported after taking hydrochlorothiazide. Pulmonary Oedema typically develops within minutes to hours after hydrochlorothiazide intake. At the onset, symptoms include dyspnoea, fever, Pulmonary deterioration and hypotension. If diagnosis of ARDS is suspected, Irbesartan and Hydrochlorothiazide should be withdrawn and appropriate treatment given. Hydrochlorothiazide should not be administered to patients who previously experienced ARDS following hydrochlorothiazide intake.

10. Interaction with other Medicaments

Interactions involving AEDs

Losartan

ACE inhibitors: The use of (active ingredient of ARB) with an ACE inhibitor may increase the risk of hyperkalaemia, hypotension, and syncope, particularly in patients with atherosclerotic disease or heart failure, or in diabetics who have end–organ damage. Such combinations should be reserved for selected cases with close monitoring of renal function.

No drug interactions occur with hydrochlorothiazide, digoxin, warfarin, cimetidine, ketoconazole, erythromycin and phenobarbital (phenobarbitone). Rifampicin and fluconazole reduce levels of active metabolite.

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 drugs which affect the excretion of sodium, lithium excretion may be reduced. Therefore, serum lithium levels should be monitored carefully if lithium salts are to be co- administered with angiotensin II receptor antagonists.

Non-steroidal anti-inflammatory drugs (NSAIDs) including selective cyclooxygenase-2 inhibitors COX-2 inhibitors) may reduce the effect of diuretics and other antihypertensive drugs. Therefore, the antihypertensive effect of angiotensin II receptor antagonists may be attenuated by NSAIDs including selective COX-2 inhibitors.

In some patients with compromised renal function who are being treated with non-steroidal anti- inflammatory drugs, including selective cyclooxygenase-2 inhibitors, the co-administration of angiotensin II receptor antagonists may result in a further deterioration of renal function. These effects are usually reversible.

Hydrochlorothiazide

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

Alcohol, barbiturates, 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.

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.

*Nonsteroidal Anti-Inflammatory Drug*s *Including Cyclooxygenase-2 Inhibitors:*
In some patients, the administration of a nonsteroidal anti-inflammatory agent including a selective cyclooxygenase-2 inhibitor 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.

11. Pregnancy & Lactation

Pregnancy

When used in pregnancy during the 2nd and 3rd trimesters, drugs that act directly on the renin-angiotensin system can cause injury and even death to the developing fetus. When pregnancy is detected, Losartan Potassium and Hydrochlorothiazide Tablets should be discontinued as soon as possible.

Although there is no experience with the use of Losartan Potassium and Hydrochlorothiazide Tablets 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 human, fetal renal perfusion, which is dependent upon the development of the renin-angiotensin system, begins in the 2nd trimester: thus, risk *to* the fetus increases if Losartan Potassium and Hydrochlorothiazide Tablets is administered during the 2nd or 3rd trimesters of pregnancy.

Use of drugs that act on the renin-angiotensin system during the second and third trimester of pregnancy reduces fetal renal function and increases fetal and neonatal morbidity and death. Resulting oligohydramnios can be associated with fetal lung hypoplasia and skeletal deformations. Potential neonatal adverse effects include skull hypoplasia, anuria, hypotension, renal failure, and death. When pregnancy is detected, discontinue Losartan Potassium and Hydrochlorothiazide Tablets as soon as possible.

These adverse outcomes are usually associated with the use of these drugs in the second and third trimesters of pregnancy. Most epidemiologic studies examining fetal abnormalities after exposure to antihypertensive use in the first trimester have not distinguished drugs affecting the renin-angiotensin system from other antihypertensive agents. Appropriate management of maternal hypertension during pregnancy is important to optimize the outcomes for both mother and fetus.

In the unusual case that there is no appropriate alternative to therapy with drugs affecting the renin-angiotensin system for a particular patient, apprise the mother of the potential risk to the fetus. Perform serial ultrasound examinations to assess the intra-amniotic environment. If oligohydramnios is observed, discontinue Losartan Potassium and Hydrochlorothiazide Tablets, unless it is considered life saving for the mother. Fetal testing may be appropriate, based on the week of pregnancy. Patients and physicians should be aware, however, that oligohydramnios may not appear until after the fetus has sustained irreversible injury. Closely observe infants with histories of in utero explosure to Losartan Potassium and Hydrochlorothiazide Tablets for hypotension, oliguria and hyperkalemia.

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 the development of toxemia of pregnancy and there is no satisfactory evidence that they are useful in the treatment of toxemia.

Lactation

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 the account the importance of the drug to the mother.

12. Side Effects

The following adverse reactions may occur:

Blood and lymphatic system disorders:
Thrombocytopenia, anemia, aplastic anaemia, haemolytic anaemia, leukopenia, agranulocytosis

Immune System disorders:
Anaphylactic reactions, angioedema including swelling of the larynx and glottis causing airway obstruction and/or swelling of the face, lips, pharynx, and/or tongue occur rarely in patients treated with Losartan; some of these patients previously experienced angioedema with other drugs including ACE inhibitors.

Metabolism and nutrition disorders:
Anorexia, hyperglycemia, hyperuricemia, electrolyte imbalance including hyponatremia and hypokalemia.

Psychiatric disorders:
Uncommon: Insomnia, restlessness

Nervous system disorders:
Dysgeusia, headache, migraine, paraesthesias.

Eye disorders:
Xanthopsia, transient blurred vision.

Cardiac disorders:
Palpitation, tachycardia.

Vascular disorders:
Dose-related orthostatic effects, necrotizing anglitis (vasculitis) (cutaneous vasculitis)

Respiratory, thoracic and mediastinal disorders:
Cough, nasal congestion, pharyngitis, sinus disorder, upper respiratory infection, Respiratory distress (including pneumonitis and pulmonary edema)

Very rare : Acute respiratory distress syndrome

Gastro-intestinal disorders:
Dyspepsia, abdominal pain, gastric irritation, cramping, diarrhea, constipation, nausea, vomiting, pancreatitis, sialoadenitis.

Hepato-biliary disorders:
Hepatitis, Jaundice (intrahepatic cholestatic jaundice).

Skin and subcutaneous tissue disorders:
Rash, pruritus, purpura (including Henoch-Schoenlein purpura), toxic epidermal necrolysis, urticaria, erythroderma, Photosensitivity, cutaneous lupus erythematotus.

Musculoskeletal and connective tissue disorders:
Back pain, muscle cramps, muscle spasm, myalgia, arthraigia.

Renal and urinary disorders:
Uncommon: Glycosuria, renal dysfunction, interstitial nephritis, renal failure.

Reproductive system and breast disorders:
Erectile dysfunction/ impotence

General disorders and administration site conditions:
Chest pain, edema/swelling, malaise, Fever, weakness.

Eye disorders:
Frequency 'not known': Choroidal effusion, acute myopia, acute angle-closure glaucoma

Investigations:
Liver function abnormalities.

Neoplasms benign, malignant and unspecified (incl cysts and polyps)
Frequency 'not known': Non-melanoma skin cancer (Basal cell carcinoma and squamous cell carcinoma)

Description of selected adverse reactions

Non-melanoma skin cancer: Based on available data from epidemiological studies, cumulative dose-dependent association between HCTZ and NMSC has been observed.

13. Symptoms and Treatment of Overdose

No specific information is available on the treatment of over dosage with Losartan Potassium and Hydrochlorothiazide. Treatment is symptomatic and supportive. Therapy with Losartan Potassium and Hydrochlorothiazide 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

The most likely manifestation of over dosage 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.

14. Shelf life

Please refer outer package for expiry date.

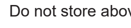
15. Special precautions for storage

Do not store above 30°C.

16. Nature and contents of container

Blister of 10 tablets and 3 such blisters are packed in a printed carton (3 x 10's) and 10 such blisters are packed in a printed carton (10 x 10's)

17. Manufactured By:



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18. Date of revision

December 2024

P1522342