LOSAR-H

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory Only

Abbreviated Prescribing information for **LOSAR-H** (Losartan Potassium and Hydrochlorothiazide Tablets I.P.) [Please refer the complete prescribing information for details].

PHARMACOLOGICAL PROPERTIES:

MECHANISM OF ACTION: ***Losartan:*** is a synthetically produced oral angiotensin-II receptor (type AT1) 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 AT1 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 AT1 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. ***Hydrochlorothiazide:*** is a thiazide diuretic. The mechanism of the antihypertensive effect of thiazide diuretics is not fully known. 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 co-administration of an angiotensin II receptor antagonist tends to reverse the potassium loss associated with thiazide diuretics.

INDICATIONS: LOSAR-H is indicated for the for treatment of mild to moderate hypertension.

DOSAGE AND ADMINISTRATION: It should be given orally Dosage: As directed by the Physician.

CONTRAINDICATION: Hypersensitivity to losartan, sulphonamide-derived substances (as hydrochlorothiazide), active substance, to any of the excipients or any other ACE (Angiotensin Converting Enzyme) inhibitors or to any of the excipients, Therapy resistant hypokalaemia or hypercalcaemia, Severe hepatic impairment; cholestasis and biliary obstructive disorders, Refractory hyponatraemia, Symptomatic hyperuricaemia/gout, 2nd and 3rd trimester of pregnancy, Severe renal impairment (i.e. creatinine clearance <30 ml/min), Anuria, The concomitant use of Losartan Potassium / Hydrochlorothiazide with aliskiren-containing, products is contraindicated in patients with diabetes mellitus or renal impairment (GFR < 60 ml/min/1.73 m_2).

WARNINGS & PRECAUTIONS: ***Losartan:*** Angioedema: Patients with a history of angioedema (swelling of the face, lips, throat, and/or tongue) should be closely monitored. Hypotension and Intravascular volume depletion: Symptomatic hypotension, especially after the first dose, may occur in patients who are volume- and/or sodium-depleted by vigorous diuretic therapy, dietary salt restriction, diarrhoea or vomiting. Such conditions should be corrected before the administration of Losartan Potassium / Hydrochlorothiazide tablets. Electrolyte imbalances: Electrolyte imbalances are common in patients with renal impairment, with or without diabetes, and should be addressed. Therefore, the plasma concentrations of potassium and creatinine clearance values should be closely monitored; especially patients with heart failure and a creatinine clearance between 30-50 ml/ min should be closely monitored. The concomitant use of potassium sparing diuretics, potassium supplements and potassium containing salt substitutes with losartan/ hydrochlorothiazide is not recommended. Liver function impairment: Based on pharmacokinetic data which demonstrate significantly increased plasma concentrations of losartan in cirrhotic patients, Losartan Potassium / Hydrochlorothiazide should be used with caution in patients with a history of mild to moderate hepatic impairment. There is no therapeutic experience with losartan in patients with severe hepatic impairment. Therefore, Losartan Potassium / Hydrochlorothiazide is contraindicated in patients with severe hepatic impairment. Renal

function impairment: As a consequence of inhibiting the renin-angiotensin-aldosterone system (RAAS), changes in renal function, including renal failure, have been reported (in particular, in patients whose renal function is dependent on the renin-angiotensin-aldosterone system, such as those with severe cardiac insufficiency or pre-existing renal dysfunction). Heart failure: In patients with heart failure, with or without renal impairment, there is - as with other medicinal products acting on the renin-angiotensin system a risk of severe arterial hypotension, and (often acute) renal impairment. In patients with heart failure, with or without renal impairment, there is - as with other medicinal products acting on the renin-angiotensin system - a risk of severe arterial hypotension, and (often acute) renal impairment. Pregnancy: AIIRAs should not be initiated during pregnancy. Unless continued AIIRA therapy is considered essential, patients planning pregnancy should be changed to alternative antihypertensive treatments which have an established safety profile for use in pregnancy. When pregnancy is diagnosed, treatment with AIIRAs should be stopped immediately, and, if appropriate, alternative therapy should be started. Dual blockade: of the renin-angiotensin-aldosterone system (RAAS) There is evidence that the concomitant use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren increases the risk of hypotension, hyperkalaemia and decreased renal function (including acute renal failure). Dual blockade of RAAS through the combined use of ACEinhibitors, angiotensin II receptor blockers or aliskiren is therefore not recommended. ***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. Metabolic and endocrine effects: Thiazide therapy may impair glucose tolerance. Dose adjustment of antidiabetic agents, including insulin, may be required. Latent diabetes mellitus may become manifest during thiazide therapy. Hepatic impairment: Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, as it may cause intrahepatic cholestasis, and since minor alterations of fluid and electrolyte balance may precipitate hepatic coma.

DRUG INTERACTIONS: *Losartan* Rifampicin and fluconazole have been reported to reduce levels of active metabolite, As with other medicinal products 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. Co-medication is not advisable, As with other medicinal products 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. ***Hydrochlorothiazide:***

Alcohol, barbiturates, narcotics or antidepressants: Potentiation of orthostatic hypotension may occur.
Antidiabetic medicinal products (oral agents and insulin): The treatment with a thiazide may influence the glucose tolerance. Dose adjustment of the antidiabetic medicinal product may be required. Metformin should be used with caution because of the risk of lactic acidosis induced by possible functional renal failure linked to hydrochlorothiazide, Carbamazepine, Iodine Contrast Media, Amphotericin B (parenteral), corticosteroids, ACTH, stimulant laxatives, or glycyrrhizin (found in liquorice).

ADVERSE REACTIONS: Most common adverse reactions are Hepatitis, Hyperkalaemia, elevation of ALT, muscle cramp, back pain, leg pain, myalgia, headache, dizziness, insomnia, renal impairment, renal failure, hyperkalaemia, mild reduction of haematocrit and haemoglobin, hypoglycaemia, Cephalalgia, asthenia, fatigue, chest pain, abdominal pain, nausea, diarrhea, dyspepsia,

MARKETED BY:

TORRENT PHARMACEUTICALS LTD.

IN/ LOSAR-H 50, 12.5 mg/Apr-2020/01/ABPI
(Additional information is available on request)