

LISTRIL PLUS

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

Abbreviated Prescribing information for LISTRIL PLUS [Lisinopril and Hydrochlorothiazide Tablets]
[Please refer the complete prescribing information available at www.torrentpharma.com]

PHARMACOLOGICAL PROPERTIES:

MECHANISM OF ACTION: *Lisinopril:* Lisinopril is a peptidyl dipeptidase inhibitor. It inhibits the angiotensin converting enzyme (ACE) that catalyses the conversion of angiotensin I to the vasoconstrictor peptide, angiotensin II. Angiotensin II also stimulates aldosterone secretion by the adrenal cortex. Inhibition of ACE results in decreased concentrations of angiotensin II which results in decreased vasopressor activity and reduced aldosterone secretion. *Hydrochlorothiazide:* Hydrochlorothiazide is a diuretic and an antihypertensive agent. It affects the distal renal tubular mechanism of electrolyte reabsorption and increases excretion of sodium and chloride in approximately equivalent amounts. Natriuresis may be accompanied by some loss of potassium and bicarbonate.

INDICATIONS: The management mild moderate hypertension in patients who have been stabilized on the individual components given in the same proportions.

DOSAGE AND ADMINISTRATION: The usual dosage is one tablet, administered once daily. As with all other medication taken once daily, Listril Plus should be taken at approximately the same time each day. In general, if the desired therapeutic effect cannot be achieved in a period of 2 to 4 weeks at this dose level, the dose can be increased to two tablets administered once daily.

CONTRAINDICATION: Hypersensitivity to lisinopril, hydrochlorothiazide or to any of the excipients or any other angiotensin converting enzyme (ACE) inhibitor. Hypersensitivity to any sulphonamide-derived drugs. History of angioedema associated with previous ACE inhibitor therapy. Hereditary or idiopathic angioedema. Second and third trimesters of pregnancy. Severe renal impairment (creatinine clearance < 30 ml/min). Anuria. Severe hepatic impairment. The concomitant use of Listril Plus with aliskiren-containing products is contraindicated in patients with diabetes mellitus or renal impairment (GFR < 60 ml/min/1.73 m²).

WARNINGS & PRECAUTIONS: Patients taking HCTZ should be informed of 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. Symptomatic hypotension is rarely seen in uncomplicated hypertensive patients but is more likely to occur if the patient has been volume-depleted, e.g. by diuretic therapy, dietary salt restriction, dialysis, diarrhoea or vomiting, or has severe renin-dependent hypertension. As with other ACE inhibitors, lisinopril should be given with caution to patients with mitral valve stenosis and obstruction in the outflow of the left ventricle such as aortic stenosis or hypertrophic cardiomyopathy. Dual blockade of RAAS through the combined use of ACE inhibitors, angiotensin II receptor blockers or aliskiren is therefore not recommended. Lisinopril/hydrochlorothiazide should not be administered to patients with renal insufficiency. The diuretic therapy should be discontinued for 2-3 days prior to initiation with lisinopril/hydrochlorothiazide. The use of lisinopril/hydrochlorothiazide is not indicated in patients requiring dialysis for renal failure. In rare occasions, patients treated with ACE inhibitors during low-density lipoprotein (LDL) apheresis with dextran sulfate have shown life threatening anaphylactic reactions. Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte balance may precipitate hepatic coma. Dosage adjustment of antidiabetic agents, including insulin, may be required. Neutropenia and agranulocytosis are reversible after discontinuation of the ACE inhibitor.

DRUG INTERACTIONS: Concomitant use of glyceryl trinitrate and other nitrates or other vasodilators may further reduce the blood pressure. Concomitant treatment of ACE inhibitors with mammalian target of rapamycin (mTOR) inhibitors or neutral endopeptidase (NEP) inhibitors or tissue plasminogen activator may increase the risk of angioedema. The combination of lisinopril and hydrochlorothiazide with lithium is therefore not recommended and careful monitoring of serum lithium levels should be performed if the combination proves necessary. The potassium losing effect of thiazide diuretics is usually attenuated by the potassium conserving effect of lisinopril. Because of the risk of hypokalaemia the concomitant administration of hydrochlorothiazide

and medicinal products that induce torsades de pointes, e.g. some antiarrhythmics, some antipsychotics and other drugs known to induce torsades de pointes, should be used with caution. NSAID and ACE inhibitors may exert an additive effect on the increase in serum potassium and may result in a deterioration of renal function. Postural hypotension may become aggravated by simultaneous intake of alcohol, barbiturates or anaesthetics.

ADVERSE REACTIONS: *Lisinopril*: Decreases in haemoglobin, decreases in haematocrit, Bone marrow depression, anaemia, thrombocytopenia, leucopenia, neutropenia, agranulocytosis, haemolytic anaemia, lymphadenopathy, autoimmune disease, Anaphylactic/anaphylactoid reaction, Syndrome of inappropriate antidiuretic hormone secretion (SIADH), Hypoglycaemia, Dizziness, headache, syncope, Paraesthesia, vertigo, taste disturbance, sleep disturbances, mood alterations, depressive symptoms, Mental confusion, Olfactory disturbance, Hallucinations, Orthostatic effects, Myocardial infarction or cerebrovascular accident, possibly secondary to excessive hypotension in high risk patients, palpitations, tachycardia, Raynaud's syndrome, Flushing, Cough, Rhinitis, Bronchospasm, sinusitis, allergic alveolitis/eosinophilic pneumonia, Diarrhoea, vomiting, Nausea, abdominal pain and indigestion, Dry mouth, Pancreatitis, intestinal angioedema, Elevated liver enzymes and bilirubin, Hepatitis - either hepatocellular or cholestatic, jaundice and hepatic failure, Rash, pruritus, Hypersensitivity/angioneurotic oedema: angioneurotic oedema of the face, extremities, lips, tongue, glottis, and/or larynx, urticaria, alopecia, psoriasis, Diaphoresis, pemphigus, toxic epidermal necrolysis, Stevens- Johnson Syndrome, erythema multiforme, cutaneous pseudolymphoma, Renal dysfunction, Uraemia, acute renal failure, Oliguria/anuria, Impotence, Gynaecomastia, Asthenia, fatigue, Increases in blood urea, increases in serum creatinine, hyperkalaemia, Hyponatraemia. *Hydrochlorothiazide*: Sialadenitis, Non-melanoma skin cancer, Restlessness, depression, sleep disturbance, Necrotising angiitis, Respiratory distress, Jaundice, Muscle spasm, fever, muscle weakness.

MARKETED BY:



Torrent Pharmaceuticals Limited.

IN/LISTRIL PLUS 5, 12.5 mg/AUG-2022/07/ABPI

(Additional information is available on request)