LISORETIC

SCHEDULING STATUS S3

1. NAME OF THE MEDICINE
LISORETIC 10/12,5 tablets
LISORETIC 20/12,5 tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
LISORETIC 10/12,5: Each tablet contains lisinopril dihydrate equivalent to lisinopril 10 mg and hydrochlorothiazide 12,5 mg.
LISORETIC 20/12,5: Each tablet contains lisinopril dihydrate equivalent to lisinopril 20 mg and hydrochlorothiazide12,5 mg.

LISORETIC 10/12,5 contains sugar (mannitol 18,70 mg/tablet).
LISORETIC 20/12,5 contains sugar (mannitol 38,30 mg/tablet).

Essentially 'sodium free'.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Tablets.
LISORETIC 10/12,5: A peach coloured, round, uncoated, biconvex tablet, debossed 'LH' on one side and plain on the other.
LISORETIC 20/12,5: A white coloured, round, uncoated, biconvex tablet, debossed 'LH' on one side and score-line on the other.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
LISORETIC is indicated for the treatment of mild to moderate hypertension in patients who have been stabilised on their individual components, given in the same proportions.

4.2 Posology and method of administration
Posology
Essential hypertension:
The usual dosage is one tablet daily, taken at approximately the same time each day. It is recommended that if the desired clinical effect cannot be achieved within 2 - 4 weeks with this dosage, the dosage may be increased to a maximum of two tablets, administered once daily.

Prior treatment with diuretics:
Symptomatic hypotension may occur after the initial dose of LISORETIC; this phenomenon is most likely to occur in patients who are volume and/or salt depleted as a result of prior diuretic therapy. If possible, the diuretic therapy should be discontinued for 2 - 3 days prior to initiation of therapy with LISORETIC, or if this is not possible, lisinopril should be given alone at a low initial dose of 5 mg.

Special populations
Renal impairment:
Hydrochlorothiazide may not be a suitable diuretic for use in patients with mild to moderate renal impairment. Hydrochlorothiazide is contraindicated in severe renal impairment (creatinine clearance values of 30 mL/min or below) (see section 4.3). LISORETIC should not be used as initial therapy in any patient with renal insufficiency. In patients with creatinine clearance of >30 and <80 mL/min, LISORETIC may be used, but only after titration of the individual components.

Use in the elderly:
There is no significant difference in the efficacy and tolerability to lisinopril and hydrochlorothiazide, administered concomitantly, between elderly and younger hypertensive patients.

Paediatric population
Safety and efficacy in children have not been established.

Method of administration
For oral use. Swallow the tablet with a drink of water.

Missed dose
Medical practitioners should advise patients who forget to take LISORETIC to take a dose as soon as possible and then continue with the normal dose. Patients should not take a double dose to compensate for the missed dose.

4.3 Contraindications
LISORETIC is contraindicated in:
- hypersensitivity to lisinopril, hydrochlorothiazide or to any of the ingredients of LISORETIC
- patients with a history of previous and/or current basal cell carcinomas and/or squamous cell carcinomas of the skin and lip
- hypersensitivity to sulphonamides and sulphonamide-derived medicines
- a history of angioedema related to previous therapy with angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs). Such patients must never again be given these medicines
- hereditary or idiopathic angioedema (see section 4.4)
- hypertrophic obstructive cardiomyopathy (HOCM)
- severe renal function impairment (creatinine clearance less than 30 mL/min)
- anuria
- bilateral renal artery stenosis
- renal artery stenosis in patients with a single kidney
- aortic stenosis
- concomitant therapy with potassium sparing diuretics such as spironolactone, triamterene, amiloride
- porphyria
- hydrochlorothiazide, as in LISORETIC, should not be given to patients with Addison's disease
- lithium therapy: concomitant administration with LISORETIC may lead to toxic blood concentrations of lithium
- severe hepatic impairment
- concomitant administration with renin inhibitors such as aliskiren-containing medicines
- the concomitant use of ACE inhibitors with fluoroquinolones is contraindicated in patients with moderate to severe renal impairment (creatinine ≤ 30 mL/min) and in the elderly patients (see sections 4.4 and 4.5)
- concomitant use of LISORETIC with sacubitril/valsartan therapy. LISORETIC must not be initiated earlier than 36 hours after the last dose of sacubitril/valsartan (see sections 4.4 and 4.5)
- pregnancy and lactation.

LISORETIC contains sodium
LISORETIC contains less than 1 mmol (0,023g) sodium per tablet, that is to say essentially 'sodium free'.

4.4 Special warnings and precautions for use

Should a woman become pregnant while receiving LISORETIC, the treatment should be stopped promptly and switched to a different class of antihypertensive medicine (see sections 4.3 and 4.6).

Renal transplantation
LISORETIC should not be administered, since there is no experience with patients recently transplanted with a kidney.

Anaphylactoid reactions in haemodialytic patients
The use of LISORETIC is not indicated in patients requiring dialysis for renal failure. Anaphylactoid reactions have been reported in patients, undergoing haemodialysis procedures with certain dialysis membranes (e.g. with the high-flux membranes AN 69 and during low-density lipoprotein apheresis with dextran sulphate) and concurrent treatment with an ACE inhibitor. Consideration to the use of a different type of dialysis membrane or a different class of antihypertensive medicine should be given in these patients.

Aortic and mitral valve stenosis/hypertrophic cardiomyopathy
LISORETIC should not be given to patients with mitral valve stenosis and obstruction in the outflow of the left ventricle, such as aortic stenosis or hypertrophic cardiomyopathy (see section 4.3).

Dual blockade of the renin-angiotensin-aldosterone system (RAAS) with aliskiren-containing medicines
Dual blockade of the renin-angiotensin-aldosterone system by combining lisinopril with renin inhibitors such as aliskiren is contraindicated since there is an increased risk of hypotension, hyperkalaemia and changes in renal function (see sections 4.3 and 4.5).

Renal insufficiency
Hydrochlorothiazide, as in LISORETIC, may not be a suitable diuretic for use in patients with renal impairment and is ineffective at creatinine clearance values of 30 mL/min or below (i.e. severe renal insufficiency). LISORETIC should not be administered to patients with a creatinine clearance ≤ 80 mL/min until titration of the individual components has shown the need for the doses present in LISORETIC.
In some patients with bilateral renal artery stenosis or stenosis of the artery to a solitary kidney, who have received ACE inhibitor treatment, increases in blood urea and serum creatinine, which may be reversible upon discontinuation of therapy, have been seen. This is especially likely to occur in patients with renal insufficiency.
Some hypertensive patients with no apparent pre-existing renal disease have developed increases in blood urea and serum creatinine, when lisinopril has been given concomitantly with a diuretic. This is more likely to occur in patients with pre-existing renal impairment. Dosage reduction and/or discontinuation of the diuretic and/or lisinopril may be required. LISORETIC is contraindicated in severe renal impairment (<30 mL/min) (see section 4.3).

The concomitant use of ACE inhibitors such as LISORETIC and fluoroquinolones, may precipitate acute kidney injury in patients, especially those with moderate to severe renal impairment (creatinine ≤ 30 mL/min) and in elderly patients (see sections 4.3 and 4.5). Renal function should be assessed before initiating treatment with concomitant use of with ACE-inhibitors and fluoroquinolones.

Prior diuretic therapy
Previous diuretic therapy should be discontinued for 2 - 3 days prior to initiation with LISORETIC. If this is not possible, treatment should be started with lisinopril alone, in a 5 mg dose.

Anaphylactoid reactions related to low-density lipoproteins (LDL) apheresis
Patients treated with ACE inhibitors such as in LISORETIC during low-density lipoprotein (LDL) apheresis with dextran sulphate have shown life threatening anaphylactic reactions.
These symptoms could be avoided by temporary discontinuation of the treatment with ACE inhibitors before each apheresis.

Hepatic disease
Caution should be exercised when hydrochlorothiazide is used in patients with hepatic impairment or progressive liver disease, as minor alterations of fluid and electrolyte balance may precipitate hepatic coma in these patients. LISORETIC is contraindicated in severe hepatic impairment (see section 4.3).
Patients receiving LISORETIC, who develop jaundice or marked elevations of hepatic enzymes should discontinue LISORETIC and receive appropriate medical follow-up.

Non-melanoma skin cancer
An increased risk of non-melanoma skin cancer (NMSC) [basal cell carcinoma (BCC) and squamous cell carcinoma (SCC)] with increasing cumulative dose of hydrochlorothiazide (HCTZ) exposure has been observed in two epidemiological studies. Photosensitising actions of HCTZ could act as a possible mechanism for NMSC.
Patients taking LISORETIC 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 preventative 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 minimise the risk of skin cancer. Suspicious skin lesions should be promptly examined potentially including histological examinations of biopsies. LISORETIC should not be used by patients who have had previous and/or current basal cell carcinomas and/or squamous cell carcinomas of the skin and/or lip (see section 4.3). The use of HCTZ may also need to be reconsidered in patients who have experienced previous NMSC.

Surgery/anaesthesia
In patients undergoing major surgery or during anaesthesia with medicines that produce hypotension, lisinopril may block angiotensin II formation secondary to compensatory renin release. Should hypotension occur, and it is considered to be due to this mechanism, the hypotension can be corrected by volume expansion.

Metabolic and endocrine effects
ACE inhibitors, such as lisinopril, and hydrochlorothiazide therapy may impair glucose tolerance. Dosage adjustment of antidiabetic medicines, including insulin, may be required. Increased cholesterol and triglyceride levels may be a result of hydrochlorothiazide diuretic therapy.
Hydrochlorothiazide may precipitate hyperuricaemia and/or gout in certain patients. Due to the increase in urinary uric acid caused by lisinopril, hyperuricaemia may be attenuated by LISORETIC which contains both components.

Hypotension and electrolyte/fluid imbalance
Symptomatic hypotension has been 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-dependant hypertension (see sections 4.4 and 4.5).
Determination of serum electrolytes should be performed at appropriate intervals in such patients. Initiation of treatment and dose adjustment should be monitored under close medical supervision in patients with an increased risk of symptomatic hypotension. Particular consideration applies to patients with ischaemic heart or cerebrovascular disease as an excessive decrease in blood pressure could result in a myocardial infarction or cerebrovascular accident.
If hypotension occurs, the patient should be placed in the supine position and, if necessary, should receive an intravenous infusion of 0.9 % normal saline. A transient hypotensive response does not warrant discontinuation of further doses.
Following restoration of effective blood volume and pressure, therapy at a reduced dosage may be reinstituted; or alternatively either of the individual components may be used separately. In some patients with heart failure who have normal or low blood pressure, additional lowering of systemic blood pressure may occur with LISORETIC. This effect is anticipated and is not usually a reason to discontinue treatment. If hypotension becomes symptomatic, a reduction of dose or discontinuation of LISORETIC may be necessary.

Electrolyte imbalance
Periodic determination of serum electrolytes should be performed at appropriate intervals.
Hydrochlorothiazide can cause fluid or electrolyte imbalance (hypokalaemia, hyponatraemia, and hypochloraemic alkalosis). Warning signs of fluid or electrolyte imbalance are dryness of mouth, thirst, weakness, lethargy, drowsiness, muscle pain or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances such as nausea or vomiting. Dilutional hyponatraemia may occur in oedematous patients in hot weather. Chloride deficit is generally mild and does not require treatment. Hydrochlorothiazide has been shown to increase the urinary excretions of magnesium, which may result in hypomagnesaemia.
Decreased urinary calcium excretion caused by hydrochlorothiazide may result in intermittent and a slightly raised serum calcium concentration. Should marked hypercalcaemia occur, it may be evidence of underlying hyperparathyroidism. LISORETIC therapy should be discontinued before carrying out tests for parathyroid function (see section 4.5).

Hyperkalaemia
Elevations in serum potassium have been observed in some patients treated with ACE inhibitors, including lisinopril as in LISORETIC.
The concomitant use of potassium sparing diuretics is contraindicated (see section 4.3).
Patients at risk of developing hyperkalaemia include those with renal insufficiency, diabetes mellitus, or those using concomitant potassium supplements or potassium-containing salt substitutes, or those patients taking other medicines associated with increases in serum potassium (e.g. heparin).
If concomitant use of the above-mentioned medicines is deemed appropriate, an increased monitoring of serum potassium is recommended (see section 4.5).

Hypersensitivity/angioedema
Angioedema of the face, extremities, lips, tongue, glottis and/or larynx has been reported in patients treated with angiotensin converting enzyme inhibitors, including lisinopril. In such cases LISORETIC should be discontinued immediately and appropriate measures should be instituted to ensure complete resolution of symptoms prior to dismissing the patient. In instances where swelling has been confined only to the face and lips, the condition may resolve without treatment, although antihistamines have been useful in relieving symptoms. Even in those instances where swelling of only the tongue is involved, without respiratory distress, patients may require prolonged observation since treatment with antihistamines and corticosteroids may not be sufficient. Angioedema associated with laryngeal oedema may be fatal. Where there is involvement of the tongue, glottis or larynx, likely to cause airway obstruction, appropriate emergency therapy should be administered promptly. This may include the administration of adrenaline (epinephrine) and/or maintenance of a patient airway. The patient should be under close medical supervision until complete and sustained resolution of symptoms has occurred. These patients should never receive any ACE-inhibitor again.
Patients with a history of angioedema unrelated to ACE-inhibitor therapy may be at increased risk of angioedema while receiving an ACE-inhibitor as in LISORETIC (see section 4.3).
In patients receiving hydrochlorothiazide as in LISORETIC, sensitivity reactions may occur with or without a history of allergy or bronchial asthma.

Due to the increased risk of angioedema, concomitant use of LISORETIC with sacubitril/valsartan is contraindicated. Sacubitril/valsartan treatment must not be initiated earlier than 36 hours after the last dose of LISORETIC. LISORETIC therapy must not be initiated earlier than 36 hours after the last dose of sacubitril/valsartan (see sections 4.3 and 4.5).

Concomitant use of LISORETIC with racecadotril, mammalian target of rapamycin (mTOR) inhibitors (e.g. sirolimus, everolimus, temsirolimus) and vildagliptin may lead to an increased risk of angioedema (e.g. swelling of the airways or tongue, with or without respiratory impairment) (see section 4.5). Caution should be used when starting racecadotril, mTOR inhibitors (e.g. sirolimus, everolimus, temsirolimus) and vildagliptin in a patient already taking LISORETIC.

Systemic lupus erythematosus
Exacerbation or activation of systemic lupus erythematosus has been reported with the use of hydrochlorothiazide.

Desensitisation
Patients receiving ACE-inhibitors, such as in LISORETIC, during desensitisation treatment (e.g. hymenoptera venom) have sustained anaphylactoid reactions. These reactions may be avoided when LISORETIC is temporarily withheld but may reappear upon inadvertent re-challenge.

Neutropaenia/agranulocytosis
Neutropaenia/agranulocytosis, thrombocytopaenia and anaemia have been reported for patients receiving ACE inhibitors as in LISORETIC. In patients with normal renal function and no other complicating factors neutropaenia occurs less frequently. Neutropaenia and agranulocytosis are reversible after discontinuation of the ACE inhibitor. Lisinopril, as in LISORETIC, should be used with extreme caution in patients with collagen vascular disease, immunosuppressant therapy, treatment with allopurinol or procainamide, or a combination of these complicating factors, especially if there is pre-existing impaired renal function. Some of these patients developed serious infections, which in a few instances did not respond to intensive antibiotic therapy. If lisinopril is used in such patients, periodic monitoring of white blood cell counts is advised and patients should be instructed to report any sign of infection.

Cough
A non-productive, persistent cough has been reported with the use of ACE inhibitors including lisinopril. The cough may usually resolve after discontinuation of therapy. ACE inhibitor-induced cough should be considered as part of the differential diagnosis of cough.

Lithium
The combination of ACE inhibitors and lithium is contraindicated (see sections 4.3 and 4.5).

Anti-doping test
The hydrochlorothiazide contained in LISORETIC could produce a positive analytic result in an anti-doping test.

Photosensitivity
Cases of photosensitivity reactions have been reported with hydrochlorothiazide (see section 4.8). If photosensitivity reaction occurs during treatment, it is recommended to stop the treatment. If a re-administration of LISORETIC is deemed necessary, it is recommended to protect exposed areas from the sun or artificial UVA.

Porphyria
Safety of hydrochlorothiazide in porphyria has not been established (see section 4.3).

Acute angle-closure glaucoma
Hydrochlorothiazide, a sulphonamide, as contained in LISORETIC has been associated with an idiosyncratic reaction, resulting in acute transient myopia and acute angle-closure glaucoma. Symptoms include acute onset of decreased visual acuity or ocular pain and typically occur within hours to weeks of LISORETIC initiation.
Untreated acute angle-closure glaucoma can lead to permanent vision loss. Primarily, treatment with hydrochlorothiazide, as in LISORETIC, must be discontinued as rapidly as possible. Prompt medical or surgical treatment may need to be considered if the intraocular pressure remains uncontrolled.
Risk factors for developing acute angle-closure glaucoma may include a history of sulphonamide or penicillin allergy (see section 4.8).

Patient populations
Ethnic groups
LISORETIC causes a higher rate of angioedema in black patients than in non-black patients. Lisinopril may be less effective in lowering blood pressure in black patients than in non-black patients, possibly because of a higher prevalence of low-renin states in the black hypertensive population.

Information on excipients of LISORETIC
LISORETIC contains less than 1 mmol (0,023 g) sodium per tablet, that is to say essentially 'sodium free'.

Paediatric population
Safety and efficacy have not yet been established in children.

4.5 Interaction with other medicines and other forms of interaction
- dual blockade of the renin-angiotensin-aldosterone system by combining lisinopril with renin inhibitors is contraindicated since there is an increased risk of hypotension, hyperkalaemia and changes in renal function. The combination of LISORETIC with renin inhibitors is contraindicated (see section 4.3)
- increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with angiotensin converting enzyme inhibitors. The combination of LISORETIC with lithium is contraindicated (see sections 4.3 and 4.4)
- concomitant use of ACE inhibitors such as LISORETIC with fluoroquinolones (e.g. ciprofloxacin, moxifloxacin and levofloxacin) may precipitate acute kidney injury (see sections 4.3 and 4.4)
- concomitant use of LISORETIC with sacubitril/valsartan is contraindicated as this increases the risk of angioedema (see section 4.3 and 4.4)
- concomitant use of LISORETIC with racecadotril, mTOR inhibitors (e.g. sirolimus, everolimus, temsirolimus) and vildagliptin may lead to an increase in the risk of angioedema (see section 4.4)
- concomitant treatment with tissue plasminogen activators may increase the risk of angioedema
- the decrease in potassium caused by hydrochlorothiazide diuretics is usually attenuated by the effect of lisinopril. The use of potassium supplements, potassium-sparing agents or potassium-containing salt substitutes, especially in patients with impaired renal function, may result in a significant increase in serum potassium (see section 4.4)
- because of the risk of hypokalaemia the concomitant administration of hydrochlorothiazide and medicines that induce torsade de pointes, e.g. some antidysrhythmics, some antipsychotics and other medicines known to induce torsade de pointes, should be used with caution
- concomitant use of certain anaesthetic medicines, tricyclic antidepressants and antipsychotics with ACE inhibitors, as in LISORETIC, may result in further lowering of blood pressure
- diuretics and other hypertensive medicines may increase the hypotensive effects
- chronic administration of nonsteroidal anti-inflammatory drugs (NSAIDs) (selective cyclooxygenase-2 inhibitors, acetylsalicylic acid (aspirin) >3 g/day and non-selective NSAIDs) may reduce the antihypertensive and diuretic effect of ACE inhibitors and hydrochlorothiazide, as in LISORETIC. NSAIDs and ACE inhibitors may exert an additive effect on the increase in serum potassium and may result in a deterioration of renal function. These effects may be reversible. Acute renal failure may occur, especially in patients with compromised renal function such as the elderly or dehydrated
- nitritoid reactions (symptoms of vasodilation including flushing, nausea, dizziness and hypotension, which can be very severe) following injectable gold (for example, sodium aurothiomalate) have been reported more frequently in patients receiving LISORETIC therapy
- sympathomimetics may antagonise the antihypertensive effect of ACE inhibitors such as LISORETIC
- epidemiological studies indicate that concomitant administration of ACE inhibitors, as in LISORETIC, and antidiabetic medicines (insulins, oral hypoglycaemic agents) may cause an increased blood glucose lowering effect with risk of hypoglycaemia. This phenomenon appears to be more likely during the first weeks of combination treatment and in patients with renal impairment
- concomitant use of hydrochlorothiazide and corticosteroids, or adrenocorticotropic hormone (ACTH) may intensify electrolyte depletion and hypokalaemia
- increased serum calcium levels due to decreased excretion may occur when administered concurrently with hydrochlorothiazide, as in LISORETIC. In cases where calcium or vitamin D must be prescribed, serum calcium levels should be monitored and the dose accordingly adjusted
- hydrochlorothiazide may decrease response to pressor amines. This decrease in response is not sufficient to preclude the use of pressor amines
- the effect of non-depolarising muscle relaxants (e.g. tubocurarine chloride) may be potentiated by hydrochlorothiazide, as in LISORETIC
- concomitant administration of ACE inhibitors and hydrochlorothiazide, as in LISORETIC, with trimethoprim increases the risk of hyperkalaemia
- hydrochlorothiazide-induced hypokalaemia can increase the risk of sotalol-induced dysrhythmia
- concomitant administration of LISORETIC and allopurinol increases the risk of renal damage and can lead to an increased risk of leukopaenia
- concomitant administration of LISORETIC and ciclosporin increases the risk of renal damage and hyperkalaemia as well as increase the risk of hyperuricaemia and gout-type complications
- concomitant administration of LISORETIC and lovastatin increases the risk of hyperkalaemia
- cytostatics, immunosuppressives, procainamide – concomitant administration of LISORETIC can lead to increased risk of leukopaenia
- alcohol, barbiturates or narcotics: potentiation of orthostatic hypotension may occur
- hydrochlorothiazide may intensify electrolyte imbalance, particularly hypokalaemia during concomitant use of amphotericin B (parenteral), carbenoxolone, corticosteroids, corticotropin (ACTH) or stimulant laxatives
- concomitant use of hydrochlorothiazide with digoxin increases the risk of digitalis toxicity associated with hydrochlorothiazide-induced hypokalaemia
- cholestyramine and colestipol may delay or reduce absorption of hydrochlorothiazide.
  Therefore, LISORETIC should be taken at least 1 hour before or 4 - 6 hours after intake of these medicines
- thiazides may increase the risk of adverse effects caused by amantadine.

4.6 Fertility, pregnancy and lactation
Pregnancy
LISORETIC is contraindicated in pregnancy and lactation (see section 4.3). LISORETIC can cause foetal morbidity and death. LISORETIC passes through the placenta and can cause disturbance in foetal blood pressure regulatory mechanisms. Oligohydramnios as well as hypotension, oliguria and anuria in new-borns, have been reported after administration of LISORETIC in the second and third trimester. Cases of defective skull ossification have been observed. Prematurity and low birth mass can occur. In addition, use of LISORETIC during the first trimester of pregnancy has been associated with an increased risk of birth defects, in particular of the cardiovascular and the central nervous system (see sections 4.3 and 4.4).

Breastfeeding
It is not known whether lisinopril is distributed into human breast milk. Hydrochlorothiazide does appear in human milk.
Because of the potential for adverse effects on the infant, mothers on LISORETIC should not breastfeed their infants (see section 4.8).

Fertility
There is no fertility data with LISORETIC.

4.7 Effects on ability to drive and use machines
LISORETIC may have a mild to moderate influence on the ability to drive and use machines. Especially at the start of the treatment or when the dose is modified, and also when used in combination with alcohol, but these effects depend on the individual's susceptibility.
LISORETIC can cause side effects such as dizziness or tiredness.
During LISORETIC administration, patients should be cautioned about re-engaging in activities requiring rapid and precise responses such as driving a vehicle or operating machinery.

4.8 Undesirable effects
a. Summary of the safety profile
The most commonly reported adverse effects with the lisinopril/hydrochlorothiazide combination are cough, fatigue, dizziness, hypotension, including orthostatic hypotension and headache.
Less common were diarrhoea, nausea, vomiting, dry mouth, rash, gout, palpitations, chest discomfort, muscle cramps and weakness, paraesthesia, asthenia and impotence.

Adverse events reported with the individual components, lisinopril and hydrochlorothiazide may be potential adverse effects with LISORETIC. Adverse effects of the individual components are detailed below.

b. Tabulated list of adverse reactions
LISORETIC – Post-marketing:

System Organ Class	Frequency	Side effects
Blood and lymphatic system disorders	*Less frequent*	Anaemia, bone marrow depression, thrombocytopaenia, leukopaenia, agranulocytosis, haemolytic anaemia
Immune system disorders	*Frequency unknown*	Anaphylactic/anaphylactoid reaction
Endocrine disorders	*Less frequent*	Inappropriate antidiuretic hormone secretion
Metabolism and nutrition disorders	*Less frequent*	Hyperglycaemia, hypokalaemia, hyperuricaemia, hyperkalaemia, gout
Psychiatric disorders	*Less frequent*	Depressive symptoms
Nervous system disorders	*Frequent*	Dizziness, headache, paraesthesia
	Less frequent	Olfactory disturbance
Cardiac disorders	*Frequent*	Orthostatic effects (including hypotension), syncope
	Less frequent	Palpitations
Respiratory, thoracic and mediastinal disorders	*Frequent*	Cough
Gastrointestinal disorders	*Less frequent*	Diarrhoea, nausea, vomiting, dry mouth, pancreatitis, intestinal angioedema
Hepatobiliary disorders	*Less frequent*	Hepatitis – either hepatocellular or cholestatic, jaundice, hepatic failure. Very rarely, it has been reported that in some patients the undesirable development of hepatitis has progressed to hepatic failure. Patients receiving LISORECTIC who develop jaundice or marked elevation of hepatic enzymes should discontinue LISORETIC and receive appropriate medical follow up.
Skin and subcutaneous tissue disorders	*Frequent*	Rash
	Less frequent	Hypersensitivity/angioneurotic oedema: angioneurotic oedema of the face, extremities, lips, tongue, glottis, and/or larynx (see section 4.3 and section 4.4), cutaneous pseudolymphoma
	Frequency unknown	A symptom complex has been reported which may include one or more of the following: fever, vasculitis, myalgia, arthralgia/arthritis, a positive antinuclear antibodies (ANA), elevated red blood cell sedimentation rate (ESR), eosinophilia and leucocytosis, rash, photosensitivity or other dermatological manifestations may occur.
Musculoskeletal, connective tissue and bone disorders	*Frequent*	Muscle cramps
	Less frequent	Muscle weakness
Reproductive system and breast disorders	*Frequent*	Impotence
General disorders and administrative site conditions	*Frequent*	Fatigue, asthenia
	Less frequent	Chest discomfort
Investigations	*Frequent*	Increases in blood urea, increases in serum creatinine, increases in liver enzymes, decreases in haemoglobin
	Less frequent	Decreases in haematocrit, increases in serum bilirubin

Lisinopril:

System Organ Class	Frequency	Side effects
Blood and lymphatic system disorders	*Less frequent*	Bone marrow depression, anaemia, thrombocytopaenia, leukopaenia, agranulocytosis, neutropaenia, haemolytic anaemia, lymphadenopathy
Immune system disorders	*Less frequent*	Hypersensitivity/angioedema of the face, extremities, lips, tongue, glottis and/or larynx, skin rash, photosensitivity, alopecia, autoimmune disease
Endocrine disorders	*Less frequent*	Syndrome of inappropriate antidiuretic hormone secretion (SIADH)
Metabolism and nutrition disorders	*Less frequent*	Gout, hyperglycaemia, hypokalaemia, hyperuricaemia hyperkalaemia, pancreatitis, hyponatraemia, hypoglycaemia
Psychiatric disorders	*Less frequent*	Mood alterations, mental confusion, depressive symptoms, sleep disturbances, olfactory disturbance, hallucinations
Nervous system disorders	*Frequent*	Dizziness, headache
	Less frequent	Paraesthesia, asthenia, fatigue, syncope, vertigo, taste disturbance, hypoaesthesia
Cardiac disorders	*Less frequent*	Myocardial infarction or cerebrovascular accident, tachycardia, palpitations, chest pain
Vascular disorders	*Less frequent*	Orthostatic effects (including orthostatic hypotension), Raynaud's syndrome, flushing
Respiratory, thoracic and mediastinal disorders	*Frequent*	Cough
	Less frequent	Bronchospasm, rhinitis, sinusitis, pulmonary infiltrates, allergic alveolitis/eosinophilic pneumonia
Gastrointestinal disorders	*Less frequent*	Nausea, gastrointestinal disturbances, stomatitis, abdominal pain, indigestion, diarrhoea, vomiting, dry mouth, intestinal angioedema, pancreatitis
Hepatobiliary disorders	*Less frequent*	Hepatitis (hepatocellular or cholestatic), jaundice, elevated liver enzymes and bilirubin, hepatic failure
Skin and subcutaneous tissue disorders	*Less frequent*	Hypersensitivity/angioneurotic oedema: angioneurotic oedema of the face, extremities, lips, tongue, glottis, and/or larynx, pruritus, urticaria, psoriasis and severe skin disorders, including pemphigus, toxic epidermal necrolysis, Stevens-Johnson syndrome, erythema multiforme, alopecia, diaphoresis, cutaneous pseudolymphoma*, skin rash
Musculoskeletal, connective tissue and bone disorders	*Less frequent*	Muscle cramps
Renal and urinary disorders	*Less frequent*	Diaphoresis, uraemia, oliguria/anuria, renal dysfunction, acute renal failure, proteinuria
Reproductive system and breast disorders	*Less frequent*	Impotence, gynaecomastia
General disorders and administrative site conditions	*Less frequent*	Asthenia, fatigue

*A symptom complex has been reported which may include one or more of the following: fever, vasculitis, myalgia, arthralgia/arthritis, a positive antinuclear antibodies (ANA), elevated red blood cell sedimentation rate (ESR), eosinophilia and leucocytosis, rash, photosensitivity or other dermatological manifestations may occur.

Hydrochlorothiazide:
Adverse events reported with the use of hydrochlorothiazide alone include

System Organ Class	Frequency	Side effects
Infections and infestations	*Frequency unknown*	Sialadenitis
Neoplasms benign and malignant (including cysts and polyps)	*Frequency unknown*	Non-melanoma skin cancer (basal cell carcinoma, squamous cell carcinoma)
Blood and lymphatic system disorders	*Less frequent*	Leukopaenia, agranulocytosis, thrombocytopaenia, aplastic anaemia, haemolytic anaemia, granulocytopenia, bone marrow depression
Immune system disorders	*Less frequent*	Hypersensitivity reaction (rash, fever, pulmonary oedema, pneumonitis, anaphylaxis)
Metabolism and nutrition disorders	*Frequent*	Electrolyte imbalance
	Less frequent	Anorexia, hyperuricaemia, gout, cholecystitis, hyperglycaemia, glycosuria, hyperuricaemia, hypomagnesaemia, increases in cholesterol and triglycerides, hyponatremia, hypokalaemia, hypochloraemic alkalosis
Psychiatric disorders	*Less frequent*	Restlessness, depression
Nervous system disorders	*Frequent*	Fever, paraesthesia, hypoaesthesia, light-headedness, dizziness, headache, sleep disturbances
Eye disorders	*Less frequent*	Xanthopsia, transient blurred vision, yellow vision, acute myopia, acute angle-closure glaucoma
	Frequency unknown	Choroidal effusion
Ear and labyrinth disorders	*Frequency unknown*	Vertigo
Cardiac disorders	*Less frequent*	Postural hypotension
Vascular disorders	*Less frequent*	Orthostatic hypotension, necrotising angiitis (vasculitis, cutaneous vasculitis)
Respiratory, thoracic and mediastinal disorders	*Frequent*	Respiratory distress (including pneumonitis and pulmonary oedema)
Gastrointestinal disorders	*Frequent*	Gastric irritation, constipation
	Less frequent	Gastrointestinal disturbances, nausea, vomiting, diarrhoea, sialadenitis, intestinal ulceration, pancreatitis
Hepatobiliary disorders	*Less frequent*	Jaundice (intrahepatic cholestatic jaundice)
Skin and subcutaneous tissue disorders	*Frequent*	Skin rash
	Less frequent	Purpura, photosensitivity, urticaria, toxic epidermal necrolysis, cutaneous lupus erythematosus-like reactions, reactivation of cutaneous lupus erythematosus, systemic lupus erythematosus
Musculoskeletal, connective tissue and bone disorders	*Frequent*	Muscle spasm
	Less frequent	Muscle weakness, muscle pain and cramps
Renal and urinary disorders	*Less frequent*	Renal dysfunction, renal failure, interstitial nephritis, non-opaque urate calculi
Reproductive system and breast disorders	*Less frequent*	Sexual dysfunction
General disorders and administrative site conditions	*Less frequent*	Fever, weakness

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on the SAHPRA website.
An email can be sent directly to the company, pharmacovigilance@pharmadynamics.co.za, to ensure safety of the product.

4.9 Overdose
Signs and symptoms:
Symptoms associated with overdosage of ACE inhibitors may include hypotension, circulatory shock, electrolyte disturbances, renal failure, hyperventilation, tachycardia, palpitations, bradycardia, dizziness, anxiety and cough. The most common signs and symptoms of hydrochlorothiazide overdose observed are those caused by electrolyte depletion (hypokalaemia, hypochloraemia, hyponatremia) and dehydration resulting from excessive diuresis.
If digitalis has been used concomitantly, hypokalaemia may accentuate cardiac dysrhythmias.

Management of overdose:
Treatment is symptomatic and supportive. No specific information is available on the treatment of overdosage with LISORETIC. Therapy with LISORETIC should be discontinued and the patient should be kept under very close supervision. Suggested measures include induction of emesis, if ingestion is recent, and correction of dehydration, electrolyte imbalance and hypotension by established procedures.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Angiotensin converting enzyme inhibitor and thiazide diuretic
ATC code: C09BA03
Pharmacological classification: A 7.1.3 Other hypotensives.

LISORETIC is a fixed dose combination product of an angiotensin converting enzyme (ACE) inhibitor, lisinopril and a diuretic, hydrochlorothiazide. Both components have complementary modes of action and exert an additive antihypertensive effect.

Lisinopril
Mechanism of action:
Lisinopril is a peptidyl dipeptidase inhibitor and inhibits the angiotensin converting enzyme (ACE) that catalyses the conversion of angiotensin I to angiotensin II. Angiotensin II is a vasoconstrictor peptide which 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. Reduced aldosterone secretion may result in an increase in serum potassium concentration. The mechanism of action through which lisinopril lowers blood pressure is mainly via suppression of the renin-angiotensin-aldosterone system; however, lisinopril also has antihypertensive effects in patients with low-renin hypertension. ACE is identical to kininase II, an enzyme that degrades bradykinin. It could be possible that increased levels of bradykinin, a potent vasodilatory peptide, play a role in the therapeutic effects of lisinopril. However, this remains to be elucidated.

Hydrochlorothiazide
Mechanism of action:
Hydrochlorothiazide is a diuretic and an antihypertensive medicine. It affects the distal renal tubular mechanism of electrolyte re-absorption and increases excretion of sodium and chloride in approximately equivalent amounts. Natriuresis may be accompanied by some loss of potassium and bicarbonate. The mechanism of the antihypertensive effects of hydrochlorothiazide is unknown. Hydrochlorothiazide does not usually affect normal blood pressure.

5.2 Pharmacokinetic properties
The concomitant administration of lisinopril and hydrochlorothiazide has no clinically significant effect on the pharmacokinetics of either medicine.

Lisinopril
Absorption:
Lisinopril is absorbed slowly, variably and incompletely after oral administration. Following oral administration of lisinopril, peak serum concentrations occur within about 7 hours. The mean extent of absorption of lisinopril is approximately 25 %, based on urinary recovery. The absorption varies between individuals (6 % - 60 %) over the dose range 5 mg - 80 mg. In patients with heart failure the absolute bioavailability is reduced by approximately 16 %. The absorption of lisinopril is not affected by the presence of food in the gastrointestinal tract.

Distribution:
Lisinopril does not appear to bind to other serum proteins other than to circulating angiotensin-converting enzymes (ACE).

Elimination:
Lisinopril does not undergo metabolism and the absorbed medicine is excreted unchanged entirely in the urine. Lisinopril has an effective half-life of accumulation of 12,6 hours on multiple dosing. In healthy subjects the clearance of lisinopril is approximately 50 mL/min. A prolonged terminal phase, is shown by declining serum concentrations, probably represented by saturable binding to ACE and is not proportional to dose.

Pharmacokinetics in special patient groups
Hepatic impairment
A decrease in lisinopril absorption (about 30 % as determined by urinary recovery) occurred as a result of hepatic function impairment in cirrhotic patients. However, an approximate 50 % increase in exposure resulted, compared to healthy subjects, due to decreased clearance.

Renal impairment
Impaired renal function decreases elimination of lisinopril, which is excreted via the kidneys. This decrease only becomes clinically important when the glomerular filtration rate is below 30 mL/min.

Table 1 Pharmacokinetic parameters of lisinopril to different groups of renal patients after administration of a multiple 5 mg dose

Renal function measured by creatinine clearance	N	C_{max} (ng/mL)	T_{max} (hr)	AUC (0-24 hrs) (ng/hr/mL)	$t_{1/2}$ (hr)
> 80 mL/min	6	40,3	6	492 ± 172	6,0 ± 1,1
30 - 80 mL/min	6	36,6	8	555 ± 364	11,8 ± 1,9
5 - 30 mL/min	6	106,7	8	2228 ± 938	19,5 ± 5,2

Mean AUC was increased by 13 % only, with a creatinine clearance of 30 - 80 mL/min, while a 4 - 5-fold increase in mean AUC was observed with creatinine clearance of 5 - 30 mL/min. Lisinopril can be removed by dialysis. Plasma lisinopril concentrations decreased on average by 60 % during 4 hours of haemodialysis, with a dialysis clearance between 40 and 55 mL/min.

Heart failure
When compared to healthy subjects, patients with heart failure have a greater exposure of lisinopril (on average an increase in AUC of 125 %). However, there is reduced absorption of approximately 16 % compared to healthy subjects (based on the urinary recovery of lisinopril).

Elderly
Older patients have higher blood levels and higher values for the area under the plasma concentration time curve than younger patients (approximately a 60 % increase).

Hydrochlorothiazide
The plasma half-life of hydrochlorothiazide can vary between 5,6 - 14,8 hours. Approximately 61 % of the dose is eliminated unchanged within 24 hours.

After oral administration of hydrochlorothiazide, diuresis begins within 2 hours, peaks in about 4 hours and lasts 6 - 12 hours. Hydrochlorothiazide does cross the placental but not the blood-brain barrier.

5.3 Preclinical safety data
Lisinopril and hydrochlorothiazide are both medicines on which extensive clinical experience have been obtained, both separately and in combination. All relevant information for the prescriber is provided elsewhere in the Professional Information.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Croscarmellose sodium
Dibasic calcium phosphate dihydrate
Magnesium stearate
Mannitol
Pregelatinised maize starch
The following colourants are also used in the 10/12,5 mg tablet only: iron oxide red, iron oxide yellow.

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
36 months.

6.4 Special precautions for storage
Store at or below 25 °C. Protect from light.
Do not remove blister from the carton until required for use.

6.5 Nature and contents of container
LISORETIC 10/12,5: PVC/PVDC/aluminium blister packs of 30 tablets, contained in a printed outer carton.
LISORETIC 20/12,5: PVC/PVDC/aluminium blister packs of 30 tablets, contained in a printed outer carton.

6.6 Special precautions for disposal
No special requirements

7. HOLDER OF THE CERTIFICATE OF REGISTRATION
Pharma Dynamics (Pty) Ltd
1st Floor Grapevine House, Steenberg Office Park
Silverwood Close
Westlake, 7945
Cape Town, South Africa
Tel: +27 21 707 7000
or 0860-PHARMA (742 762)

8. REGISTRATION NUMBERS
LISORETIC 10/12,5: A37/7.1.3/0475
LISORETIC 20/12,5: A37/7.1.3/0476

9. DATE OF FIRST AUTHORISATION
Date of registration: 11 February 2005

10. DATE OF REVISION OF THE TEXT
03 March 2025

NAMIBIA
LISORETIC 10/12,5 NS2 06/7.1.3/0063
LISORETIC 20/12,5 NS2 06/7.1.3/0064

MOZAMBIQUE
LISORETIC 10/12,5: 4648
LISORETIC 20/12,5: 4649

ZAMBIA
LISORETIC 10/12,5 POM 051/021
LISORETIC 20/12,5 POM 051/020

H6211

pharma dynamics

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS S3

LISORETIC 10/12,5 tablets
LISORETIC 20/12,5 tablets
Lisinopril dehydrate and hydrochlorothiazide
LISORETIC contains sugar (mannitol 18,70 mg and 38,30 mg respectively)
Essentially 'sodium free'.

Read all of this leaflet carefully before you start taking LISORETIC
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist, nurse or other healthcare provider.
- LISORETIC has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet
1. What LISORETIC is and what it is used for
2. What you need to know before you take LISORETIC
3. How to take LISORETIC
4. Possible side effects
5. How to store LISORETIC
6. Contents of the pack and other information

1. What LISORETIC is and what it is used for
Lisinopril belongs to a group of medicines called angiotensin converting enzyme inhibitors (ACEI). It works by making your blood vessels wider.
Hydrochlorothiazide belongs to a group of medicines called diuretics (water tablets). It helps your body get rid of water and salts, like sodium, in your urine.

LISORETIC is used to treat mild to moderate high blood pressure (hypertension).
Your doctor will usually prescribe LISORETIC when your blood pressure has already been controlled after taking both the individual active ingredients of this medicine separately.

2. What you need to know before you take LISORETIC
Do not take LISORETIC:
- if you are hypersensitive (allergic) to lisinopril, hydrochlorothiazide, or any of the other ingredients of LISORETIC (see section 6)
- if you have had skin cancer or you develop an unexpected skin lesion during the treatment with LISORETIC
- if you are hypersensitive (allergic) to sulphonamides (used to treat certain infections) and medicines made from sulphonamide
- if you or anyone in your family have a history of angioedema (swellings similar to hives beneath the surface of the skin) related to previous therapy with LISORETIC or other medicines containing the same active ingredients as LISORETIC or with certain medicines used to treat heart conditions, called ACE inhibitors (angiotensin-converting enzyme inhibitors), or ARBs (angiotensin receptor blockers).
  If this is the case, you may never take these medicines again
- if you suffer from hypertrophic obstructive cardiomyopathy (HOCM – thickening of the muscle of the heart)
- if you don't pass or pass very little urine per day
- if you have anuria (a condition where your kidneys cannot produce urine, and you stop passing urine)
- if you have severe kidney disease, narrowing of the blood vessels of both kidneys, are undergoing haemodialysis or you have only one kidney left, of which the blood vessels are narrowed
- if you have a disease of the heart valves called aortic stenosis in which the opening is narrowed
- if you are also being treated with medicines called potassium sparing diuretics (e.g. spironolactone, triamterene or amiloride) that increases the rate of urination
- if you have porphyria (a rare hereditary disease in which your urine becomes dark and your skin is extremely sensitive to light)
- if you have Addison's disease (a hormone disease with symptoms such as chronic fatigue, loss of appetite and weight loss)
- if you are receiving lithium therapy (a mood stabilizer) concomitant administration with LISORETIC may lead to toxic blood concentrations of lithium
- if you have severely impaired liver function or liver cirrhosis (an advanced liver disease with symptoms such as yellowing of the skin, easy bruising and fatigue)
- if you suffer from biliary obstruction (a problem with the drainage of the bile from the gall bladder)
- if you are taking a blood pressure medicine containing aliskiren
- if you are taking antibiotic medicine containing fluoroquinolones (e.g. ciprofloxacin, levofloxacin) and have a history of moderate or severe kidney injury
- if you have taken or are currently taking sacubitril/valsartan, a medicine used to treat a type of long-term (chronic) heart failure in adults, as the risk of angioedema (rapid swelling under the skin in an area such as the throat) is increased
- if you are, or think you may be, pregnant or if you are planning to become pregnant or if you are breastfeeding.

Warnings and precautions
Take special care with LISORETIC:

If you become pregnant while taking LISORETIC, you should stop taking LISORETIC immediately and inform your doctor. He/she may have to switch you to a different medicine.

Tell your doctor if any of the following applies to you:
- if you have recently had a kidney transplant, require dialysis or have renal failure
- if you are being treated with a diuretic (water tablet) or are on a salt restricted diet as you may experience a serious drop in blood pressure (hypotension)
- if you have a heart condition called mitral valve stenosis (narrowing of a heart valve causing a blockage in blood flow)
- if you suffer from a hormonal disorder called primary aldosteronism
- if you take a medicine called aliskiren as this may lower your blood pressure (see Other medicines with LISORETIC)
- if you have kidney problems
- if you are taking antibiotics called fluoroquinolones (e.g. ciprofloxacin, levofloxacin), the combined use with LISORETIC may increase the risk of sudden and severe kidney injury, especially if you have moderate or severe kidney impairment such as in elderly patients
- if you are on any other water tablets as this needs to be stopped before taking LISORETIC
- if you have high levels of cholesterol and you are having a treatment called 'low-density lipoprotein (LDL)' apheresis (a process to remove cholesterol from the blood)
- if you have liver problems, which include symptoms such as yellowing of the skin and eyes
- since treatment with hydrochlorothiazide as in LISORETIC, particularly long-term use with high doses, may increase the risk of some types of skin and lip cancer (non-melanoma skin cancer), protect your skin from sun exposure and UV rays while taking LISORETIC
- if you are about to undergo major surgery or anaesthetic
- if you have gout
- if you experience fatigue, muscle weakness, drowsiness, nausea, vomiting or cramps as these may be symptoms of a condition called electrolyte imbalance. Your doctor may want to do regular blood tests
- if you are about to have a thyroid test
- if you experience swelling in any part of your body
- if you have ever had a condition called systemic lupus erythematosus (SLE) with symptoms such as joint pain, extreme fatigue and a rash over the nose and cheeks)
- if you are taking sacubitril/valsartan (used to treat chronic heart failure), your doctor will change the frequency of therapy
- if you are taking medicines called mammalian target of rapamycin (mTOR) inhibitors (for example temsirolimus, everolimus, sirolimus) or medicines containing neprilysin inhibitors (NEP) (for example racecadotril) as they may increase the risk of angioedema (swelling of the face, lips, tongue and/or throat with difficulty in swallowing or breathing)
- if you have problems with your blood vessels (collagen vascular disease)
- if you are about to undergo desensitisation therapy (due to an allergy e.g. insect bites). If you take LISORETIC while you are having this treatment, it may cause a severe allergic reaction
- if you suffer from an arthritis type disease called collagen vascular disease
- if you develop an infection
- as a continuous cough may develop while taking LISORETIC. The cough may usually stop when you complete your LISORETIC treatment
- if you develop sensitivity to the sun e.g. your skin becomes itchy or reddens and swelling occurs when exposed to the sun. Inform your healthcare provider about any reactions to the sun. Should your health provider advise you to continue with LISORETIC, it is necessary to protect exposed areas of your body from the sun
- if you experience visual disturbances or pressure in the eyes, severe eye pain, headaches, nausea and vomiting, and your eyes are constantly tearing
- if you are a black patient as LISORETIC may not effectively lower your blood pressure. You may also more easily get the side effect "angioedema" (a severe allergic reaction with swelling of the hands, feet, ankles, face, lips, tongue or throat)
- hydrochlorothiazide contained in LISORETIC could produce a positive result in an anti-doping test.

Children
The safety and efficacy of LISORETIC in children has not yet been established.

Other medicines and LISORETIC
Always tell your healthcare provider if you are taking any other medicine. (This includes complementary or traditional medicines.)

LISORETIC can interact with the following medicines:
- lithium, may result in toxic blood concentrations if used in combination with LISORETIC (see Do not take LISORETIC)
- other medicines from the same class (angiotensin-II receptor antagonists or ACE inhibitors) to lower blood pressure, including those that contain aliskiren
- other water tablets or medicines to lower your blood pressure may increase effects of LISORETIC to lower your blood pressure, you may experience symptoms such as light-headedness or dizziness, fainting, nausea, fatigue and lack of concentration. Inform your doctor if you are taking any of these
- potassium supplements or salt substitutes containing potassium (these may lead to increased potassium concentrations in the blood)
- medicines that alter the heart rate and certain medicines used to treat mental conditions, antidepressants and certain anaesthetic medicines, as this may lower your blood pressure below normal (discuss with your doctor if you are unsure)
- certain medicines used to treat pain and inflammation called NSAIDs (nonsteroidal anti-inflammatory drugs e.g. aspirin) as the effect of LISORETIC may be reduced
- medicines that contain gold, such as sodium aurothiomalate, which may be given to you as an injection, may cause flushing of the skin, nausea and light-headedness
- medicines called sympathomimetics, used to treat nose or sinus congestion or other cold remedies (including those you can buy in the pharmacy), may prevent LISORETIC from lowering your blood pressure
- medicines used to treat diabetes (e.g. metformin, insulin and diazoxide), when taken together with LISORETIC, may significantly reduce your blood sugar levels which might lead to hypoglycaemia, you may experience symptoms such as dizziness, headaches and mood changes
- corticosteroids (used to reduce inflammation, suppress the immune system, and replacement therapy)
- calcium containing medicines and vitamin D supplements may increase calcium levels in the blood resulting in dehydration, fatigue, loss of appetite or thirst
- pressor amines, e.g. adrenaline (epinephrine) used for the treatment of hypotension, shock, cardiac failure, asthma or allergies, may become less effective when used together with LISORETIC
- muscle relaxants (e.g. tubocurarine), as the effect of these medicines may be increased when used together with LISORETIC
- certain antibiotics (such as trimethoprim) and medicines which reduce high cholesterol (such as lovastatin), may increase the risk of low blood potassium levels, which may include symptoms such as weakness, fatigue, tingling and numbness and breathing difficulties
- medicines for the treatment of gout or muscular pain (such as indomethacin or allopurinol) may cause the risk of a decreased urine output or fluid retention and may lower your immune system
- medicines to suppress the body's immune response (immunosuppressants, such as ciclosporin), NSAIDs and anticonvulsion medicines to treat seizures (such as ACE inhibitors) may cause decreased urine output, fluid retention, causing swelling in your legs and the risk of low blood potassium which may cause symptoms such as weakness, fatigue, tingling and numbness and breathing difficulties
- medicines used to control heart rhythm (such as procainamide) and those used for chemotherapy for cancer (such as cytostatics), may lower your immune system and you may become more prone to infection
- amphotericin B injection (used to treat fungal infections), carbenoxolone (used to treat ulcers or inflammation in or around the mouth), corticosteroids (steroid medicines), corticotropin (a hormone) or stimulant laxatives (medicines used to treat constipation) may intensify your electrolyte imbalance which may cause symptoms such as irregular heartbeat, fatigue, nausea, vomiting, diarrhoea or constipation
- medicines used to treat heart failure (digoxin) increase the risk of digitalis toxicity which may cause symptoms such as fatigue, malaise and visual disturbances
- medicines used to lower cholesterol (cholestyramine and colestipol) may delay the absorption of LISORETIC, therefore LISORETIC should be taken at least 1 hour before or 4 - 6 hours after taking these medicines
- antibiotic medicines called fluoroquinolones ciprofloxacin, moxifloxacin and levofloxacin) may increase the risk of sudden and severe kidney injury
- sedatives, narcotics or excessive alcohol may lead to further lowering of blood pressure, which is suddenly triggered by a change in posture, such as when a person stands up quickly
- sacubitril/valsartan (used to treat chronic heart failure) increases the risk of angioedema (a severe allergic reaction with swelling of the hands, feet, ankles, face, lips, tongue or throat) (see Do not take LISORETIC and Warnings and precautions)
- medicines which are most often used to avoid rejection of transplanted organs (temsirolimus, sirolimus, everolimus and other medicines belonging to the class of mTOR inhibitors) (see Warnings and precautions)
- medicines to break up blood clots (tissue plasminogen activator), usually given in hospital.

LISORETIC with food and drink
LISORETIC can be taken with or without food.

Pregnancy, breastfeeding and fertility
If you are pregnant or breastfeeding your baby, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before taking LISORETIC.

You should not take LISORETIC if you are pregnant or breastfeeding (see Do not take LISORETIC).

LISORETIC is not recommended in early pregnancy, and must not be taken when more than 3 months pregnant, as it may cause serious harm to your baby if used after the third month of pregnancy.

Treatment with LISORETIC is not recommended during breast-feeding (see Do not take LISORETIC).

Driving and using machines
As with other blood pressure lowering medicines, LISORETIC may have a mild to moderate influence on the ability to drive and use machines. Especially at the start of the treatment or when the dose is modified, and also when used in combination with alcohol, but these effects depend on the individual's susceptibility.
Medicines which lower blood pressure may cause dizziness or drowsiness.
It is not always possible to predict to what extent LISORETIC may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which LISORETIC affects them.

LISORETIC contains sodium
LISORETIC contains less than 1 mmol sodium (0,023 g) per tablet, that is to say essentially 'sodium free'.

3. How to take LISORETIC
Do not share medicines prescribed for you with any other person.
Always take LISORETIC exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Adults
The usual dose is one tablet once daily, taken at the same time every day with or without food.
The dose of LISORETIC can be increased to 2 tablets per day, depending on your blood pressure response. Your doctor will decide on the dose depending on your condition. The tablets should be swallowed with sufficient fluid.

Patients on diuretic (water tablets) therapy
Inform your doctor if you are taking water tablets as he/she may want to stop your water tablet before starting you on LISORETIC therapy.

Patients with severe kidney disease
LISORETIC is not recommended for patients with severe kidney problems (see Do not take LISORETIC).

Use in the elderly
No dosage reduction is usually necessary in the elderly.

Children
LISORETIC is not recommended for use in children and adolescents due to a lack of data on safety and efficacy.

Your doctor will tell you how long your treatment with LISORETIC will last. Do not stop treatment early because your high blood pressure may return.
If you have the impression that the effect of LISORETIC is too strong or too weak, tell your doctor or pharmacist.

If you take more LISORETIC than you should
In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

Symptoms of overdose may include:
- hypotension (dizziness, fainting, nausea), rapid breathing (hyperventilating), pale or sweaty skin, bluish lips and nails (circulatory shock), decreased urine output, fluid retention, causing swelling in your legs, ankles or feet, abnormally slow, fast or irregular heart rate or anxiety and cough.

The most common signs of overdosage, related to decreased electrolytes in the body, are weakness, tiredness, cramping of muscles, tingling or numbness, bloating or constipation, dehydration, diarrhoea or vomiting, confusion, seizures and dehydration due to frequent passing of urine. Your healthcare provider will advise you on precautionary measures to take in the case of overdose.

If you forget to take LISORETIC
If you forget to take LISORETIC, take one as soon as you remember. If it is almost time for your next dose, skip the missed dose and continue to take the tablet or tablets at the usual time. Do not take a double dose to make up for forgotten individual doses.

If you stop taking LISORETIC
It is important that you continue the course of treatment even if you begin to feel better after a few days.

4. Possible side effects
LISORETIC can have side effects.
Not all side effects reported for LISORETIC are included in this leaflet. Should your general health worsen, or if you experience any untoward effects while using LISORETIC, please consult your doctor, pharmacist or other healthcare professional for advice.

If any of the following happens, stop using LISORETIC and tell your doctor immediately or go to the casualty department at your nearest hospital:
- swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing
- rash or itching
- fainting.

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to LISORETIC. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:
- fever, unexplained wide spread of skin pain, red or purple rash that spreads or blisters on your skin and the mucous membranes of your mouth, nose, eyes, genitals or shedding of your skin within days after blisters form which are symptoms for Stevens-Johnson syndrome
- jaundice (yellow discolouration of the skin and eyes)
- heart attack or stroke
- increased or fast heartbeat (tachycardia)
- low blood pressure or fainting when getting up from a lying or sitting position (orthostatic hypotension/dizziness)
- chest pain (angina)
- weakness, fatigue, weight loss, headache (symptoms of a condition called vasculitis)
- kidney problems (passing less urine than is normal for you)
- hepatitis (inflammation of the liver with symptoms such as nausea, mild fever, abdominal pain).

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:
Frequent side effects:
- dizziness, headache
- cough
- changes in the levels of certain chemicals in the blood and urine which are usually detected by blood and urine tests (electrolyte imbalance)
- vertigo (loss of balance), dizziness, tingling sensation in hands, feet or lips (feeling of "pins and needles"), sleep disturbances, light-headedness
- stomach pain or discomfort, constipation
- skin rash.

Less frequent side effects:
- increased immune response (autoimmune disease)
- problems with your bone marrow or a reduced number of blood cells and/or platelets in your blood. You may notice tiredness, an infection (which may be serious), fever, feeling breathless or that you bruise or bleed more easily
- changes to some of the cells or other parts of your blood, abnormal blood test results including anaemia
- low levels of sugar in your blood (hypoglycaemia)
- pancreatitis (inflammation of the pancreas with symptoms such as stomach pain, increased heart rate and fever)
- deficiency of potassium, sodium and magnesium, increased cholesterol levels and excess of uric acid in the bloodstream (seen through blood tests)
- insomnia, sleep disturbances, mood changes, anxiety, depression, confusion, hallucinations (seeing or hearing things that are not there), restlessness, changes to your sense of smell
- flushing, change of colour in your fingers or toes
- upper respiratory tract infections, nasal congestion, sinus disorders, sore throat
- stomach pain or discomfort, inflammation of the stomach, bloating, flatulence (gas)
- wind, stomach spasms, inflammation of a salivary gland
- diarrhoea, vomiting, dry mouth, nausea, indigestion
- abnormal liver function (clay coloured stool, dark urine, itching, loss of appetite, yellow eyes or skin), liver failure
- muscle cramps, spasms, weakness or pain
- hives, itching, inflammation of the skin, rash, redness of the skin, sensitivity to light, dry skin, blistering or peeling of the skin, hair loss
- abnormal kidney function including inflammation of the kidneys, urinary infection, sugar in the urine, increased protein levels in the urine, liver failure
- blurred vision, worsening eyesight, seeing things in yellow
- problems with your sight for a short time, eye pain with redness
- vertigo (loss of balance)
- problems with sexual performance, enlarged breasts in men.

The following side effects have been reported but the frequency for them to occur is not known:
- skin and lip cancer (non-melanoma skin cancer), with abnormal growth of skin, bump or sores on the lips that persist for a long period of time
- inflammation of a salivary gland
- sudden eye pain and visual loss.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on the SAHPRA website.
By reporting side effects, you can help provide more information on the safety of LISORETIC. You can also send an email directly to the company, pharmacovigilance@pharmadynamics.co.za, to ensure safety of the product.

5. How to store LISORETIC
Store all medicines out of reach of children.
Store at or below 25 °C.
Protect from light.
Keep blisters in carton until required for use.
Do not use after the expiry date stated on the carton.
Return all unused medicine to your pharmacist.
Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information
What LISORETIC contains:
The active ingredients are lisinopril and hydrochlorothiazide.
LISORETIC 10/12,5: Each tablet contains lisinopril dihydrate equivalent to lisinopril 10 mg and hydrochlorothiazide 12,5 mg.
LISORETIC 20/12,5: Each tablet contains lisinopril dihydrate equivalent to lisinopril 20 mg and hydrochlorothiazide 12,5 mg.

The other ingredients are:
Tablet cores:
Croscarmellose sodium, dibasic calcium phosphate dihydrate, magnesium stearate, mannitol, pregelatinised maize starch.
The following colourants are also used in the 10/12,5 mg tablet only: iron oxide red, iron oxide yellow.

What LISORETIC looks like and contents of the pack
LISORETIC 10/12,5: A peach coloured, round, uncoated, biconvex tablet, debossed 'LH' on one side and plain on the other.
LISORETIC 20/12,5: A white coloured, round, uncoated, biconvex tablet, debossed 'LH' on one side and score-line on the other.

LISORETIC 10/12,5 and LISORETIC 20/12,5 are packed into PVC/PVDC/aluminium blister packs of 30 tablets, contained in a printed outer carton.

Holder of Certificate of Registration
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This leaflet was last revised in
03 March 2025

Registration numbers
LISORETIC 10/12,5: A37/7.1.3/0475
LISORETIC 20/12,5: A37/7.1.3/0476

NAMIBIA
LISORETIC 10/12.5: NS2 06/7.1.3/0063
LISORETIC 20/12.5: NS2 06/7.1.3/0064

MOZAMBIQUE
LISORETIC 10/12.5: 4648
LISORETIC 20/12.5: 4649

ZAMBIA
LISORETIC 10/12.5: POM 051/021
LISORETIC 20/12.5: POM 051/020

H6211

PASIËNTINLIGTINGSBLAD

SKEDULERINGSTATUS S3

LISORETIC 10/12,5 tablette
LISORETIC 20/12,5 tablette
Lisinoprildehidraat en hidrochloortiasied
LISORETIC bevat suiker (mannitol 18,70 en 38,30 mg onderskeidelik)
Wesenlik 'natriumvry'.

Lees hierdie hele inligtingsblad noukeurig deur, voordat u begin om LISORETIC te neem.
- Hou hierdie inligtingsblad. Dit mag nodig wees vir u om dit weer te lees.
- Indien u verdere vrae het, vra asseblief u dokter, apteker, verpleegkundige, of ander gesondheidsorgverskaffer.
- LISORETIC is vir u persoonlik voorgeskryf en u moet nie u medisyne met ander mense deel nie. Dit mag skadelik wees vir hulle, selfs al is hulle simptome dieselfde as u eie.

Inhoud van hierdie inligtingsblad
1. Wat LISORETIC is en waarvoor dit gebruik word
2. Wat u nodig het om te weet, voordat u LISORETIC neem
3. Hoe om LISORETIC te neem
4. Moontlike newe-effekte
5. Hoe om LISORETIC te bewaar
6. Verpakkingsinhoud en ander inligting

1. Wat LISORETIC is en waarvoor dit gebruik word
Lisinopril behoort aan 'n groep medisyne wat angiotensienomsettingsensiem inhibitors (AOEI) genoem word. Dit werk deurdat dit u bloedvate verwyd.
Hidrochloortiasied behoort aan 'n groep medisyne wat diuretika (watertablette), genoem word. Dit help u liggaam om ontslae te raak van water en soute soos natrium, deur u urine.
LISORETIC word gebruik om lig tot matige hoë bloeddruk (hipertensie), te behandel. U dokter sal gewoonlik LISORETIC voorskryf, wanneer u bloeddruk alreeds onder beheer is, nadat beide die individuele aktiewe bestanddele van hierdie medisyne, voorheen afsonderlik gebruik was.

2. Wat u nodig het om te weet, voordat u LISORETIC neem
Moet nie LISORETIC neem:
- indien u hipersensitief (allergies) is vir lisinopril, hidrochloortiasied, of enige van die ander bestanddele van LISORETIC nie (sien afdeling 6)
- indien u velkanker gehad het, of 'n onverwagte velletsel tydens die behandeling met LISORETIC, ontwikkel nie
- indien u hipersensitief (allergies) is vir sulfoonamiede (gebruik om sekere infeksies te behandel) en medisyne wat van sulfoonamiede afkomstig is nie
- indien u, of enige iemand in u familie 'n geskiedenis van angio-edeem (swellings soortgelyk aan urtikarie onder die veloppervlakte), verwant aan vorige behandeling met LISORETIC, of ander medisyne wat dieselfde aktiewe bestanddele as LISORETIC bevat, of met sekere medisyne wat gebruik word om harttoestande te behandel en AOEIs (angiotensienomsettingsensiem inhibitors) genoem word, of ARBs (angiotensien reseptorblokkers), het nie. Indien dit die geval is, mag u nooit weer hierdie medikasie neem nie
- indien u aan hipertrofiese obstruktiewe kardiomiopatie (HOKM – verdikking van die hartspier), ly nie
- indien u daagliks baie min, of glad nie, urineer nie
- indien u anurie het nie ('n toestand waar u niere nie urine kan vervaardig nie en u ophou om te urineer)
- indien u aan 'n erge niersiekte, vernouing van die bloedvate van beide niere ly nie, indien u hemodialise ondergaan nie, of slegs een nier, waarvan die bloedvate vernou is, het nie
- indien u 'n hartklepsiekte, wat aortiese stenose genoem word en waar die opening vernou is, het nie
- indien u ook met medisyne wat kaliumsparende diuretika genoem word (bv. spironolaktoon, triamtereen, of amiloried), wat die tempo van urinering verhoog, behandel word nie
- indien u porfirie het nie ('n skaars oorerflike siekte, waar u urine donker voorkom en u vel uiters sensitief vir lig is)
- indien u Addison se siekte het nie ('n hormoonsiekte met simptome soos chroniese uitputting, aptytverlies en gewigsverlies)
- indien u litiumbehandeling ('n gemoedstabiliseerder), saam met die gelyktydige gebruik van LISORETIC, ontvang nie, aangesien dit mag lei tot toksiese bloedkonsentrasies van litium
- indien u aan erg belemmerde lewerfunksie, of lewersirrose ly nie ('n gevorderde lewersiekte met simptome soos vergeling van die vel, maklike kneusing en uitputting)
- indien u aan biliêre obstruksie ly nie ('n probleem met die dreinering van die gal vanuit die galblaas)
- indien u bloeddrukmedikasie wat aliskiren bevat, neem nie
- indien u antibiotiese medisyne wat fluoorkinolone bevat (bv. siprofloksasien, levofloksasien) neem en 'n geskiedenis van matige of erge nierskade het nie
- indien u tans of onlangs sakubitril/valsartan neem of geneem het nie ('n medisyne wat gebruik word om 'n tipe langtermyn (chroniese) hartversaking by volwassenes te behandel), aangesien die risiko vir angio-edeem (vinnige swelling onder die vel by 'n gedeelte soos die keel), mag toeneem
- indien u swanger is, vermoed dat u swanger mag wees, swangerskap beplan, of borsvoed nie.

Waarskuwings en voorsorgmaatreëls
Neem spesiale sorg met LISORETIC:

Indien u swanger raak, terwyl u LISORETIC neem, moet u die gebruik daarvan onmiddellik staak en u dokter inlig. Hy/sy mag dit nodig ag, om u na 'n ander medisyne oor te skakel.

Vertel u dokter, indien enige van die volgende op u van toepassing is:
- indien u onlangs 'n nieroorplanting gehad het, dialise benodig, of nierversaking het
- indien u tans met 'n diuretikum (watertablet) behandel word, of op 'n soutbeperkende dieet is, aangesien u 'n ernstige afname in bloeddruk (hipotensie), mag ervaar
- indien u aan 'n harttoestand wat mitrale klepstenose genoem word, ly (vernouing van 'n hartklep, wat 'n blokkasie in bloedvloei veroorsaak)
- indien u aan 'n hormonale versteuring, wat primêre aldosteronisme genoem word, ly
- indien u medisyne wat aliskiren genoem word neem, aangesien dit u bloeddruk mag verlaag (sien Ander medisyne saam met LISORETIC)
- indien u nierprobleme het
- indien u antibiotika wat fluoorkinolone (bv. siprofloksasien, levofloksasien) genoem word, neem. Die gesamentlike gebruik met LISORETIC mag die risiko vir skielike en erge nierbeskadiging verhoog, veral indien u, soos by bejaardes, matige tot erge nierbelemmering het
- indien u enige ander watertablette neem, aangesien dit gestaak moet word, voordat LISORETIC gebruik begin word
- indien u hoë cholesterolvlakke het en u behandeling, wat 'laedigtheidslipoproteïen (LDL)' aferese genoem word, ondergaan ('n prosedure om cholesterol vanuit die bloed te verwyder)
- indien u lewerprobleme het, wat simptome soos vergeling van die vel en oë insluit
- aangesien behandeling met hidrochloortiasied (soos bevat in LISORETIC), veral langtermyngebruik teen hoë doserings, die risiko vir sommige tipes vel- en lipkanker (nie-melanoomvelkanker) mag verhoog, moet u u vel teen sonblootstelling en UV-strale beskerm, terwyl u LISORETIC neem
- indien u binnekort 'n groot operasie moet ondergaan, of narkose moet ontvang
- indien u jig het
- indien u uitputting, spierswakheid, lomerigheid, naarheid, braking, of krampe ervaar, aangesien dit simptome van 'n toestand wat elektrolietwanbalans genoem word, mag wees. U dokter mag dit nodig ag om gereelde bloedtoetse uit te voer
- indien u 'n skildkliertoets binnekort beplan
- indien u swelling in enige gedeelte van u liggaam ervaar
- indien u ooit aan 'n toestand wat sistemiese lupus erythematosus (SLE) genoem word gely het, met simptome soos gewrigspyn, uiterste moegheid en 'n uitslag oor die neus en wange
- indien u sakubitril/valsartan neem (gebruik om chroniese hartversaking te behandel), sal u dokter die frekwensie van behandeling, aanpas
- indien u medisyne wat soogdierteiken van rapamisien (mTOR) inhibitors genoem word, neem (byvoorbeeld temsirolimus, everolimus, sirolimus), of medisyne wat neprilisien (NEP) inhibitors bevat (byvoorbeeld rasekadotril), aangesien dit die risiko vir angio-edeem (swelling van die gesig, lippe, tong en/of keel, saam met moeisame sluk of asemhaling), mag verhoog
- indien u probleme met u bloedvate het (kollagene vaskulêre siekte)
- indien u binnekort desensitasiebehandeling moet ondergaan (weens 'n allergie bv. insekbyte). Indien u LISORETIC neem, terwyl u hierdie behandeling ondergaan, mag dit 'n erge allergiese reaksie veroorsaak
- indien u aan 'n artritis-tipe siekte ly, wat kollagene vaskulêre siekte genoem word
- indien u 'n infeksie ontwikkel
- aangesien 'n voortdurende hoes mag ontwikkel terwyl u LISORETIC neem. Die hoes mag gewoonlik opklaar, wanneer u u LISORETIC behandeling voltooi
- indien u 'n sensitiwiteit teenoor die son ontwikkel bv. u vel begin jeukerig en rooi word en swelling kom voor na sonblootstelling. Lig u gesondheidsorgverskaffer in omtrent enige reaksies teenoor die son. Sou u gesondheidsorgverskaffer aanraai dat u voortgaan met LISORETIC, maak seker dat u enige gedeeltes van u liggaam wat blootgestel word aan die son, beskerm
- indien u enige sigsteurnisse, of druk in die oë, erge oogpyn, hoofpyn, naarheid en braking en oë wat voortdurend traan, ervaar
- indien u 'n swart pasiënt is, aangesien LISORETIC nie u bloeddruk doeltreffend mag verlaag nie. U mag ook die newe-effek "angio-edeem" ('n erge allergiese reaksie met swelling van die hande, voete, enkels, gesig, lippe, tong, of keel), makliker ondervind
- hidrochloortiasied, soos bevat in LISORETIC, mag 'n positiewe anti-dwelmtoets lewer.

Kinders
Die veiligheid en doeltreffendheid van LISORETIC by kinders, is nog nie vasgestel nie.

Ander medisyne en LISORETIC
Vertel altyd u gesondheidsorgverskaffer indien u enige ander medisyne neem (dit sluit aanvullende, of tradisionele medisyne in).

LISORETIC kan wisselwerkings met die volgende medisyne toon:
- litium, mag lei tot toksiese bloedkonsentrasies, indien dit in kombinasie met LISORETIC geneem word (sien Moet nie LISORETIC neem)
- ander medisyne vanuit dieselfde klas (angiotensien-II reseptorantagoniste, of AOE inhibitors) om bloeddruk te verlaag, insluitend die wat aliskiren bevat
- ander watertablette of medisyne wat u bloeddruk verlaag, mag die uitwerking van LISORETIC om u bloeddruk te verlaag, versterk. U mag simptome soos lighoofdigheid, of duiseligheid, floute, naarheid, uitputting en konsentrasieverlies, ervaar. Lig u dokter in, indien u enige van hierdie medikasie neem
- kaliumaanvullings, of soutvervangers wat kalium bevat (dit mag lei tot verhoogde kaliumkonsentrasies in die bloed)
- medisyne wat die harttempo verander en sekere medisyne wat gebruik word om geestestoestande te behandel, antidepressante en sekere narkosemiddels, aangesien dit bloeddruk laer as normaal mag verlaag (bespreek met u dokter indien u onseker is)
- sekere medisyne wat gebruik word om pyn en inflammasie te behandel en NSAIMs genoem word (niesteroïdale anti-inflammatoriese middels), aangesien die effek van LISORETIC verswak mag word
- medisyne wat goud bevat, soos natriumourotiomalaat, wat as 'n inspuiting aan u toegedien mag word, aangesien dit blosvorming van die vel, naarheid en lighoofdigheid mag veroorsaak
- medisyne wat simpatomimetika genoem word en gebruik word om neus-, of sinuskongestie te behandel, of ander verkouemiddels (insluitend dit wat u in die apteek kan koop), mag verhoed dat LISORETIC u bloeddruk verlaag
- medisyne wat gebruik word om diabetes te behandel (bv. metformien, insulien en diasoksied) en saam met LISORETIC geneem word, mag u bloedsuikervlakke beduidend verlaag en mag lei tot hipoglisemie. U mag simptome soos duiseligheid, hoofpyne en gemoedsveranderinge ervaar
- kortikosteroïede (gebruik om inflammasie te verminder, die immuunstelsel te onderdruk en as vervangingsterapie)
- kalsiumbevattende medisyne en vitamien D aanvullings, mag die kalsiumvlakke in die bloed verhoog en lei tot dehidrasie, uitputting, aptytverlies, of dors
- pressor-amiene bv. adrenalien (epinefrien), wat gebruik word vir die behandeling van hipotensie, skok, hartversaking, asma, of allergieë, mag minder doeltreffend raak, wanneer dit saam met LISORETIC gebruik word
- spierverslappers (bv. tubukurarien). Die effek van hierdie medisyne mag versterk word, wanneer dit saam met LISORETIC geneem word
- sekere antibiotika (soos trimetopriem) en medisyne wat hoë cholesterol verlaag (soos lovastatien), mag die risiko vir lae bloedkaliumvlakke verhoog en simptome soos swakheid, uitputting, tinteling en gevoelloosheid en asemhalingsprobleme tot gevolg hê
- medisyne vir die behandeling van jig, of spierpyn (soos indometasien of allopurinol), mag die risiko vir 'n afname in urinering, of vloeistofretensie verhoog en u immuunstelsel verswak
- medisyne wat die liggaam se immuunrespons onderdruk (immunodepressante, soos siklosporien), NSAIMs en stuipwerende medisyne, wat aanvalle behandel (soos AOE inhibitors), mag 'n afname in urinering, vloeistofretensie, wat swelling in u bene tot gevolg het veroorsaak en die risiko vir lae bloedkalium wat simptome soos swakheid, uitputting, prikkeling en gevoelloosheid en asemhalingsprobleme insluit, verhoog
- medisyne wat gebruik word om die hartritme te beheer (soos prokaïenamied) en dit was as chemoterapie vir kanker gebruik word (soos sitostatika), mag u immuunstelsel verswak en u mag 'n groter neiging vir infeksies toon
- amfoterasien B inspuiting (gebruik om swaminfeksies te behandel), karbenoksoloon (gebruik om sere of inflammasie in en rondom die mond te behandel), kortikosteroïede (steroïedmedisyne), kortikotropien ('n hormoon), of stimulant lakseermiddels (medisyne wat gebruik word om hardlywigheid te behandel), mag u elektrolietwanbalans vererger en simptome soos onreëlmatige hartklop, uitputting, naarheid, braking, diarree, of hardlywigheid veroorsaak
- medisyne wat gebruik word om hartversaking te behandel (digoksien), verhoog die risiko vir digitalistoksisiteit, wat simptome soos uitputting, malaise en sigsteurnisse mag veroorsaak
- medisyne wat gebruik word om cholesterol te verlaag (cholestiramien en kolestipol), mag die absorpsie van LISORETIC vertraag en dus moet LISORETIC ten minste 1 uur voor, of 4 - 6 uur na hierdie medisyne geneem word
- antibiotiese medisyne wat fluoorkinolone genoem word (siprofloksasien, moksifloksasien en levofloksasien), mag die risiko vir skielike en erge nierbeskadiging, verhoog
- sedeermiddels, narkotika, of oormatige alkoholverbruik, mag lei tot verdere verlaging van bloeddruk, wat skielik mag voorkom deur 'n postuurverandering, soos wanneer 'n persoon vinnig opstaan
- sakubitril/valsartan (gebruik om chroniese hartversaking te behandel), verhoog die risiko vir angio-edeem ('n erge allergiese reaksie met swelling van die hande, voete, enkels, gesig, lippe, of keel) (sien Moet nie LISORETIC neem en Waarskuwings en voorsorgmaatreëls)
- medisyne wat mees algemeen gebruik word om verwerping van oorgeplante organe te verhoed (temsirolimus, sirolimus, everolimus en ander medisyne wat aan die klas mTOR inhibitors behoort) (sien Waarskuwings en voorsorgmaatreëls)
- medisyne om bloedklonte op te breek (weefselplasminogeen aktiveerder), gewoonlik in 'n hospitaal toegedien.

LISORETIC saam met kos en drinkgoed
LISORETIC kan saam met, of sonder kos geneem word.

Swangerskap, borsvoeding en fertiliteit
Indien u swanger is of u baba borsvoed, vermoed dat u swanger is, of 'n baba beplan, raadpleeg asseblief u dokter, apteker, of ander gesondheidsorgverskaffer vir advies, voordat LISORETIC gebruik word.

U moet nie LISORETIC neem indien u swanger is, of borsvoed nie (sien Moet nie LISORETIC neem).

LISORETIC word nie aanbeveel tydens vroeë swangerskap nie en moet nie geneem word indien u langer as 3 maande swanger is nie, aangesien dit ernstige skade aan u baba mag berokken na die derde maand van swangerskap.

Behandeling met LISORETIC word nie aanbeveel tydens borsvoeding nie (sien Moet nie LISORETIC neem).

Bestuur en die hantering van masjiene
Soos met ander bloeddrukverlagende medisyne, mag LISORETIC 'n lig tot matige invloed op die vermoë om te bestuur en masjiene te hanteer, uitoefen. Veral met die aanvang van behandeling, of wanneer die dosis aangepas word en ook wanneer dit in kombinasie met alkohol gebruik word. Hierdie effekte hang af van die individu se vatbaarheid.
Medisyne wat bloeddruk verlaag, mag duiseligheid of lomerigheid veroorsaak.
Dit is nie altyd moontlik om te voorspel tot watter mate LISORETIC met die daaglikse aktiwiteite van 'n pasiënt sal inmeng nie. Pasiënte moet verseker dat hulle nie betrokke raak by bogenoemde aktiwiteite totdat hulle bewus is hoe LISORETIC hulle aantas nie.

LISORETIC bevat natrium
LISORETIC bevat minder as 1 mmol (0,023 g) natrium per tablet, dit wil sê wesenlik 'natriumvry'.

3. Hoe om LISORETIC te neem
Moet nie medisyne wat vir u voorgeskryf is met enige ander persoon deel nie.
Neem LISORETIC altyd presies soos deur u dokter aanbeveel word. U moet u dokter of apteker raadpleeg indien u onseker is.

Volwassenes
Die gewone dosis is een tablet een keer daagliks, op dieselfde tyd elke dag, saam met, of sonder kos.
Die LISORETIC dosis kan verhoog word na 2 tablette per dag, in ooreenstemming met u bloeddrukreaksie. U dokter sal besluit op die dosis, afhangende van u toestand. Die tablette moet met 'n voldoende hoeveelheid vloeistof gesluk word.

Pasiënte op diuretika (watertablette) behandeling
Lig u dokter in, indien u watertablette neem, aangesien hy dit nodig mag ag om u watertablet te staak, voordat u met LISORETIC behandeling begin.

Pasiënte met erge niersiekte
LISORETIC word nie aanbeveel vir pasiënte met erge nierprobleme nie (sien Moet nie LISORETIC neem).

Gebruik deur bejaardes
Geen dosisaanpassing word gewoonlik benodig vir bejaardes nie.

Kinders
LISORETIC word nie aanbeveel vir gebruik deur kinders en adolessente, weens die tekort aan data, wat verband hou met die veiligheid en doeltreffendheid daarvan, nie.

U dokter sal vir u aandui hoe lank u behandeling met LISORETIC sal duur. Moet nie behandeling vroegtydig staak nie, aangesien u hoë bloeddruk mag terugkeer.
Indien u onder die indruk is dat die uitwerking van LISORETIC té sterk, of té swak is, vertel u dokter of apteker.

Indien u meer LISORETIC neem as wat u behoort
In die geval van oordosering, raadpleeg u dokter of apteker. Indien beide nie beskikbaar is nie, kontak die naaste hospitaal, of gifbeheersentrum.

Simptome van oordosering mag die volgende insluit:
- hipotensie (duiseligheid, flouwording, naarheid), vinnige asemhaling (hiperventilasie), bleek of sweterige vel, blouerige lippe en naels (sirkulatoriese skok), afname in urinering, vloeistofretensie, wat swelling in u bene, enkels, of voete veroorsaak, abnormaal stadige, vinnige, of onreëlmatige hartklop, of angstigheid en hoes.

Die mees algemene tekens van oordosering wat verband hou met 'n afname in elektroliete in die liggaam, is swakheid, moegheid, spierkrampe, prikkeling of gevoelloosheid, opgeblasenheid of konstipasie, dehidrasie, diarree of braking, verwarring, aanvalle en dehidrasie weens gereelde urinering. U gesondheidsorgverskaffer sal u advies gee, omtrent die voorsorgmaatreëls om te tref in die geval van oordosering.

Indien u vergeet om LISORETIC te neem
Indien u vergeet om LISORETIC te neem, neem dit so gou as wat u onthou. Indien dit egter amper tyd is vir u volgende dosis, slaan die vergete dosis oor en hou aan om die tablet, of tablette, op die gewone tydstip te neem. Moet nie 'n dubbeldosis neem om op te maak vir die vergete, individuele doserings nie.

Indien u die gebruik van LISORETIC staak
Dit is belangrik dat u die behandelingskursus volhou, selfs al begin u beter voel na etlike dae.

4. Moontlike newe-effekte
LISORETIC kan newe-effekte hê.
Nie alle newe-effekte wat vir LISORETIC aangemeld is, word in hierdie inligtingsblad ingesluit nie. Sou u algemene gesondheid versleg, of indien u enige ongunstige effekte ervaar, terwyl u LISORETIC gebruik, raadpleeg asseblief u dokter, apteker, of ander gesondheidsorgdeskundige vir advies.

Indien enige van die volgende gebeur, staak die gebruik van LISORETIC en vertel u dokter onmiddellik, of gaan na die ongevalle-afdeling by u naaste hospitaal:
- swelling van die hande, voete, enkels, gesig, lippe, mond of keel, wat moeisame sluk of asemhaling mag veroorsaak
- uitslag of gejeuk
- floute.

Hierdie is alles baie ernstige newe-effekte. Indien u dit ondervind, kon u 'n ernstige allergiese reaksie teenoor LISORETIC ervaar het. U mag dringende mediese aandag, of hospitalisasie benodig.

Vertel u dokter onmiddellik, of gaan na die ongevalle-afdeling by u naaste hospitaal, indien u enige van die volgende opmerk:
- koors, onverklaarbare wydverspreide velpyn, rooi, of pers uitslag wat versprei, of blase wat vorm op die vel en slymvliesmembrane van die mond, neus oë of geslagsdele, of afskilfering van die vel binne etlike dae nadat die blase gevorm het. Dit is simptome van Stevens-Johnson-sindroom
- geelsug (geel verkleuring van die vel en oë)
- hartaanval of beroerte
- verhoogde, of vinnige hartklop (tagikardie)
- lae bloeddruk, of flouwording wanneer u opstaan vanuit 'n lêende of sittende posisie (ortostatiese hipotensie/duiseligheid)
- borspyn (angina)
- swakheid, uitputting, gewigsverlies, hoofpyn (simptome van 'n toestand wat vaskulitis genoem word)
- nierprobleme (urineer minder as waaraan u gewoond is)
- hepatitis (inflammasie van die lewer, met simptome soos naarheid, ligte koors, buikpyn).

Hierdie is alles ernstige newe-effekte. U mag dringende mediese aandag benodig.

Vertel u dokter indien u enige van die volgende opmerk:
Algemene newe-effekte:
- duiseligheid, hoofpyn
- hoes
- veranderinge in die vlakke van sekere chemiese stowwe in die bloed en urine, wat gewoonlik deur bloed- en urientoetse opgespoor word (elektrolietwanbalans)
- vertigo (balansverlies), duiseligheid, prikkelende sensasie in die hande, voete, of lippe (gevoel van "spelde en naalde"), slaapsteurnisse, lighoofdigheid
- maagpyn of -ongemak, hardlywigheid
- veluitslag.

Minder algemene newe-effekte:
- verhoging in immuunreaksie (outo-immuunsiekte)
- probleme met u beenmurg, of afname in die hoeveelheid bloedselle en/of plaatjies in u bloed. U mag moegheid opmerk, 'n infeksie (wat ernstig mag wees), koors, asemnood, of dat u makliker kneus of bloei
- veranderinge aan sommige van die selle, of ander gedeeltes van u bloed, abnormale bloedtoetsresultate, insluitend anemie
- lae suikervlakke in u bloed (hipoglisemie)
- pankreatitis (inflammasie van die pankreas, met simptome soos maagpyn, verhoogde hartklop en koors)
- tekort aan kalium, natrium en magnesium, verhoogde cholesterolvlakke en 'n oormaat uriensuur in die bloedstroom (bepaal deur bloedtoetse)
- insomnie, slaapsteurnisse, gemoedsveranderinge, angstigheid, depressie, verwarring, hallusinasies (sien of hoor dinge wat nie werklik is nie), rusteloosheid, veranderinge in u reuksensasie
- blosvorming, verandering in die kleur van u vingers of tone
- boonste lugweginfeksies, neusstuwing, sinusversteurings, seer keel
- maagpyn, of -ongemak, maaginflammasie, voel opgeblaas, flatulensie (winderigheid)
- winderigheid, maagspasmas, inflammasie van 'n speekselklier
- diarree, braking, droë mond, naarheid, indigestie
- abnormale lewerfunksie (klei-kleurige stoelgang, donker urine, gejeuk, aptytverlies, geel oë of vel), lewerversaking
- spierkrampe, spasmas, swakheid of pyn
- urtikarie, gejeuk, inflammasie van die vel, uitslag, rooiheid van die vel, ligsensitiwiteit, droë vel, blaasvorming of afskilfering van die vel, haarverlies
- abnormale nierfunksie, insluitend inflammasie van die niere, urinêre infeksie, suiker in die urine, verhoogde proteïenvlakke in die urine, lewerversaking
- wasige visie, sig wat versleg, sien dinge in 'n geel skynsel
- korttermyn sigprobleme, oogpyn, met rooiheid
- vertigo (balansverlies)
- probleme met seksuele optrede, vergrote borste by mans.

Die volgende newe-effekte is aangemeld, maar die frekwensie van voorkoms is onbekend:
- vel- en lipkanker (nie-melanoomvelkanker), met abnormale velgroei, knoppe of sere op die lippe wat volhard oor 'n lang tydperk
- inflammasie van die speekselklier
- skielike oogpyn en sigverlies.

Indien u enige newe-effekte opmerk, wat nie in hierdie inligtingsblad genoem word nie, lig asseblief u dokter of apteker in.

Aanmelding van newe-effekte

Indien u newe-effekte ervaar, praat met u dokter, apteker of verpleegkundige. U kan ook newe-effekte aanmeld by SAHPRA via die Med Safety toepassing (Medsafety X SAHPRA) en eReporting platform (who-umc.org), wat op SAHPRA se webtuiste gevind kan word. Deur die aanmelding van newe-effekte, kan u help om meer inligting aangaande die veiligheid van LISORETIC in te win. U kan ook 'n epos direk aan die maatskappy stuur, pharmacovigilance@pharmadynamics.co.za, om die veiligheid van die produk te verseker.

5. Hoe om LISORETIC te bewaar
Bewaar alle medisyne buite die bereik van kinders.
Bewaar teen of benede 25 °C.
Beskerm teen lig.
Hou stulpstroke in die kartonhouer, totdat dit benodig word vir gebruik.
Moet nie gebruik na die vervaldatum wat op die kartonhouer aangedui word nie.
Neem alle ongebruikte medisyne na u apteker terug.
Moet nie ongebruikte medisyne in afvoerpype of rioolstelsels (bv. toilette) weggooi nie.

6. Verpakkingsinhoud en ander inligting
Wat LISORETIC bevat:
Die aktiewe bestanddele is lisinoprildihidraat en hidrochloortiasied.
LISORETIC 10/12,5: Elke tablet bevat lisinoprildihidraat gelykstaande aan lisinopril 10 mg en hidrochloortiasied 12,5 mg.
LISORETIC 20/12,5: Elke tablet bevat lisinoprildihidraat, gelykstaande aan lisinopril 20 mg en hidrochloortiasied 12,5 mg.

Die ander bestanddele is
Tabletkerne:
Dibasiese kalsiumfosfaatdihidraat, kruisgekoppelde natriumkarmellose, magnesiumstearaat, mannitol, vooraf-gegelatineerde mieliestysel.
Die volgende kleurmiddels word ook gebruik in die 10/12,5 mg tablet alleenlik: geel ysteroksied, rooi ysteroksied.

Hoe LISORETIC lyk en die verpakkingsinhoud
LISORETIC 10/12,5: 'n Perskekleurige, ronde, onbedekte, bikonvekse tablet, gedebosseleer 'LH' aan een kant en glad aan die teenoorgestelde kant.
LISORETIC 20/12,5: 'n Witkleurige, ronde, onbedekte, bikonvekse tablet, gedebosseleer 'LH' aan een kant en gegroef aan die teenoorgestelde kant.

LISORETIC 10/12,5: word verpak in PVC/PVDC/aluminiumstulpverpakkings van 30 tablette, in 'n gedrukte buitenste kartonhouer.

Eienaar van die Registrasiesertifikaat
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Hierdie inligtingsblad was voorheen hersien
03 March 2025

Registrasienommers
LISORETIC 10/12,5: A37/7.1.3/0475
LISORETIC 20/12,5: A37/7.1.3/0476

NAMIBIË
LISORETIC 10/12,5: NS2 06/7.1.3/0063
LISORETIC 20/12,5: NS2 06/7.1.3/0064

MOSAMBIEK
LISORETIC 10/12,5: 4648
LISORETIC 20/12,5: 4649

ZAMBIË
LISORETIC 10/12,5: POM 051/021
LISORETIC 20/12,5: POM 051/020

H6211