LIZRO
P1525214

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P1525214

PROFESSIONAL INFORMATION
SCHEDULING STATUS
SOUTH AFRICA: S3
NAMIBIA: NS2

NOVAGEN PHARMA

1. NAME OF THE MEDICINE
LIZRO 5 mg (Tablets)
LIZRO 10 mg (Tablets)
LIZRO 20 mg (Tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
LIZRO 5 mg: Each tablet contains 5,44 mg lisinopril dihydrate equivalent to anhydrous lisinopril 5 mg.
LIZRO 10 mg: Each tablet contains 10,87 mg lisinopril dihydrate equivalent to anhydrous lisinopril 10 mg.
LIZRO 20 mg: Each tablet contains 21,74 mg lisinopril dihydrate equivalent to anhydrous lisinopril 20 mg.

LIZRO contains sugar (i.e. mannitol).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Tablets

LIZRO 5 mg: Light red coloured, round shaped, biconvex, uncoated tablets, debossed with ‘L’ on one side and on other side with ‘5’ on one side of the score line.
LIZRO 10 mg: Light yellow coloured, round shaped, biconvex, uncoated tablets, debossed with ‘L’ on one side and on other side with ‘10’.
LIZRO 20 mg: Light yellow coloured, capsule shaped, biconvex, uncoated tablets, debossed with ‘L’ on one side and on other side with ‘20’.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications
LIZRO is indicated for the treatment of:
- Mild to moderate hypertension – alone or in combination with other antihypertensives.
- Congestive heart failure – as adjunctive therapy with diuretics and where appropriate, digitalis.
- Acute myocardial infarction – LIZRO administered within 24 hours to haemodynamically stable patients reduces the risk of left ventricular dysfunction or heart failure.

4.2 Posology and method of administration
May be taken with/without meals preferably at the same time every day.

Mild to Moderate hypertension:
Adults: Initial dose is 10 mg per day given as a single dose. The dose should be adjusted according to blood pressure response. The usual effective maintenance dose is 20 mg per day, given as a single dose with a maximum of 40 mg per day.
The full therapeutic effect may take several weeks. Therefore, if the desired effect has not been achieved within 2 to 4 weeks the dose may be increased.

Congestive Heart Failure:
Adults: Initial dose is 2,5 mg per day as a single dose. This may be increased at intervals of 4 weeks until the therapeutic effect is reached. Adjustments should be based on clinical response. Maintenance dosing range is 5 mg to 20 mg per day administered as a single dose.

Acute Myocardial Infarction:
Adults: 5 mg within 24 hours of the onset of an acute myocardial infarction, followed by 5 mg after 24 hours of the first dose, 10 mg after 48 hours of the first dose and then 10 mg per day for six weeks.
In patients with low systolic blood pressure (less than or equal to 120 mmHg), an initial dose of 2,5 mg should be used during the first three days after the infarction. If hypotension occurs (systolic blood pressure less than or equal to 100 mmHg), a daily maintenance dose of 5 mg may be given with temporary reductions of 2,5 mg if needed. If prolonged hypotension occurs (systolic blood pressure less than 90 mmHg for more than 1 hour) LIZRO should be withdrawn.

Dosing in high risk individuals:
Diuretic-treated patients: In order to minimise the possibility of sudden and severe hypotension which may occur within the first 1 to 5 hours after the initial dose of LIZRO, diuretics should be discontinued 2 to 3 days before beginning therapy with LIZRO. In patients where diuretic therapy cannot be discontinued, treatment with LIZRO should be initiated with a 5 mg dose. Subsequent dosage adjustments will depend on the therapeutic response. If required, diuretic therapy may be resumed.

Renal impairment: A lower dose is required. If creatinine clearance is 31 ml - 70 ml/min the starting dose is 5 mg to 10 mg per day. The dose may be increased as needed according to therapeutic response to a maximum of 20 mg per day.

Renovascular hypertension: Dose should be lowered to 2,5 mg or 5 mg and the patient should be monitored.
LIZRO is not affected by the presence of food. LIZRO should be administered as a single daily dose at approximately the same time every day.

4.3 Contraindications
- Sensitivity to any of the components of LIZRO.
- A history of angioedema related to previous therapy with ACE inhibitors or angiotensin receptor blockers (ARBs): These patients must never again be given these medicines.
- Hereditary or idiopathic angioedema.
- Aortic stenosis.
- Hypertrophic obstructive cardiomyopathy (HOCM).
- Moderate to severe renal function impairment (creatinine clearance less than 30 ml/min).
- Bilateral renal artery stenosis.
- Renal artery stenosis in patients with a single kidney.
- Concomitant therapy with potassium sparing diuretics such as spironolactone, triamterene and amiloride.
- Porphyria.
- Thiazide diuretics in (fixed dose) combination with LIZRO should not be given to patients with Addison’s disease. This therapy is also contraindicated in patients with severe renal impairment or anuria, and in patients who show hypersensitivity to other sulphonamide-derived medicines.
- Lithium therapy: Concomitant administration with LIZRO may lead to toxic blood concentrations of lithium.
- Pregnancy and lactation (see section 4.4 and 4.6)
- The concomitant use of LIZRO with aliskiren-containing products is contraindicated.
- Concomitant use of fluoroquinolones with ACE inhibitors as contained in LIZRO is contraindicated in patients with moderate to severe renal impairment.

4.4 Special warnings and precautions for use

Should a woman become pregnant while receiving LIZRO, the treatment must be stopped promptly and switched to a different class of medicine. (See section 4.3 and 4.6). If a woman is contemplating pregnancy, a different class of medicine should be used. (See section 4.3 and 4.6).

LIZRO should be used with caution in the following conditions:
- Cerebrovascular disease or ischaemic heart disease - Reduction in blood pressure could aggravate these conditions and may result in myocardial infarction and cerebrovascular accidents.
- Volume depleted patients (e.g. by diuretic therapy, dietary salt restriction, dialysis, diarrhoea or vomiting).
  Although it may occur in normovolemic patients, hypotension is more likely in volume depleted patients. A sudden reduction in angiotensin II may result in sudden and severe hypotension. There is also an increased risk of LIZRO induced renal failure, especially in those with congestive heart failure. In volume depleted patients or patients with ischaemic heart disease or cerebrovascular disease, therapy should be monitored, especially when the dose of LIZRO or diuretic is adjusted.
- There is evidence that the concomitant use of ACE-inhibitors, angiotensin II receptor blockers (ARBs) or aliskiren may increase the risk of hypotension, hyperkalaemia and decreases renal function (including acute renal failure). Dual blockade of RAAS through the combined use of LIZRO and aliskiren is therefore contraindicated (see section 4.3).
- Patients at a high risk of symptomatic hypotension e.g. patients with salt or volume depletion with or without hyponatremia should have these conditions corrected before therapy with LIZRO. Monitoring is required after initiating therapy. If hypotension occurs, the patient should be placed in the supine position and if necessary receive an intravenous infusion of 0,9 % saline.
- In patients undergoing major surgery or during anaesthesia with medicines that produce hypotension, LIZRO may block angiotensin II formation secondary to complementary renin release. If hypotension occurs and is considered to be due to this mechanism, it can be corrected by volume expansion.
- Severe autoimmune disease, especially systemic lupus erythematosus, other collagen vascular disease or scleroderma: Increase the risk for development of neutropenia or agranulocytosis.
- In acute myocardial infarction, treatment with LIZRO should not be initiated in patients with evidence of renal dysfunction (serum creatinine concentrations exceeding 177 micromol/L or proteinuria exceeding 500 mg/24 hours). If renal dysfunction develops during treatment (serum creatinine concentrations exceeding 177 micromol/L or doubling of the pre-treatment value) then LIZRO may need to be withdrawn.
- In acute myocardial infarction, patients may develop persistent hypotension and/or impaired renal function.
- Hypotension in acute myocardial infarction - Treatment with LIZRO must not be initiated in acute myocardial infarction patients who are at risk of further serious haemodynamic deterioration after treatment with a vasodilator. These include patients with systolic blood pressure of 100 mmHg or lower or cardiogenic shock. During the first 3 days following the infarction, the dose should be reduced if the systolic blood pressure is 120 mmHg or lower. Maintenance doses should be reduced to 5 mg or temporarily to 2,5 mg if systolic blood pressure is 100 mmHg or lower. If hypotension persists (systolic blood pressure less than 90 mmHg for more than 1 hour) then LIZRO should be withdrawn.
- Bone marrow depression - Increased risk of agranulocytosis and neutropenia.
- Diabetes mellitus - Increased risk of hyperkalaemia, as well as hypoglycaemia may occur.
- Hyperkalaemia - LIZRO may cause an increase in serum potassium levels.
- Renovascular disease - LIZRO should not be used in patients with renovascular disease or suspected renovascular disease but it may be used cautiously in severe resistant hypertension in such patients. In this instance, LIZRO should only be used under specialist supervision. The elderly patients with peripheral vascular diseases or generalised atherosclerosis may have asymptomatic renovascular disease. (See section 4.2).
- Renal artery stenosis, bilateral or in one kidney or renal transplant - Increased risk of renal function impairment may cause increases in blood urea and serum creatinine concentrations, which may be reversible upon discontinuation of therapy. There is also an increased risk of agranulocytosis and neutropenia when immunosuppressants are concurrently administered.
- Renal function impairment - Decreased elimination of LIZRO resulting in an increased risk of hyperkalaemia. These patients may require lower doses.
- Increases in blood urea and serum creatinine have been seen in patients with no apparent pre-existing vascular disease, especially when LIZRO has been given concomitantly with a diuretic. Dosage reduction or discontinuation of LIZRO or the diuretic may be required.
- Concomitant use of mTOR inhibitors (e.g. sirolimus, everolimus and temsirolimus): Patients taking concomitant mTOR inhibitors (e.g. sirolimus, everolimus and temsirolimus) therapy may be at increased risk for angioedema (e.g. swelling of the airways or tongue, with or without respiratory impairment) (see section 4.5).
- Anaphylactoid reactions have occurred in patients using ACE inhibitors during desensitising protocols involving for example, hymenoptera venom.
- Anaphylactoid reactions have been reported in patients exposed to either high-flux membrane dialysis or low-density lipoprotein apheresis with dextran sulphate absorption.
- Hypersensitivity/Angioedema - If angioedema of the face, extremities, lips, tongue, glottis and/or larynx is observed in patients treated with LIZRO**,** LIZRO should be discontinued promptly. These patients should be monitored to ensure complete resolution of symptoms.
- 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. This may include the administration of adrenaline and/or the maintenance of a patent airway. The patient should be under close medical supervision until complete and sustained resolution of symptoms has occurred. **These patients should never receive any LIZRO again.**
- LIZRO causes a higher rate of angioedema in black patients than in non-black patients.
- Porphyria: contraindicated (see section 4.3).
- Safety and efficacy in children has not been established.
- Concomitant therapy with potassium sparing diuretics such as spironolactone, triamterene and amiloride may lead to hyperkalaemia, which may be severe and lead to cardiac conduction abnormalities, dysrhythmias and cardiac arrest and is therefore contraindicated (see section 4.3).
- Cough: Cough has been reported with the use of ACE inhibitors as contained in LIZRO. Characteristically, the cough is non-productive, persistent and resolves after discontinuation of therapy. ACE inhibitor-induced cough should be considered as part of the differential diagnosis of cough.
- Very rarely, ACE inhibitors as contained in LIZRO have been associated with a syndrome that starts with cholestatic jaundice and progresses to fulminant necrosis and (sometimes) death. The mechanism of this syndrome is not understood. Patients receiving LIZRO who develop jaundice or marked elevations of hepatic enzymes should discontinue LIZRO and receive appropriate medical follow-up.
- Concomitant use of fluoroquinolone antibiotics and ACE inhibitors (as contained in LIZRO) may precipitate acute kidney injury in patients, especially those with moderate to severe renal impairment and elderly patients (see section 4.3). Renal function should be assessed before initiating treatment, and monitored during treatment, with fluoroquinolones or ACE inhibitors.

4.5 Interaction with other medicines and other forms of interaction
Concomitant use of LIZRO with:
- ARBs, ACE inhibitors, or aliskiren - Clinical trial data has shown that dual blockade of the renin-angiotensin-aldosterone-system (RAAS) through the combined use of ACE inhibitors, angiotensin II receptor blockers or aliskiren is associated with a higher frequency of adverse events such as hypotension, hyperkalaemia and decreased renal function (see sections 4.3 and 4.4).
- Diuretics, alcohol and hypotension-producing medications - The antihypertensive effect is additive. Dosage adjustments may be necessary during concurrent use or when one medicine is discontinued.
- Loop, thiazide or related diuretics - “First dose hypotension” may occur (See section 4.2).
- Indomethacin and nonsteroidal anti-inflammatory medicines (NSAIDs) - reduce the antihypertensive effects of LIZRO. Blood pressure monitoring should be increased when any NSAID is added or discontinued in a patient treated with LIZRO**.**
- Potassium supplements or potassium sparing diuretics such as spironolactone, triamterene or amiloride - concurrent administration may result in hyperkalaemia.
- Lithium - Increases in lithium concentrations have been reported. Frequent monitoring of serum lithium concentrations is recommended.
- Gold - Nitritoid reactions (symptoms of vasodilatation 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 ACE inhibitor therapy.
- Tricyclic antidepressants/Antipsychotics/Anaesthetics - Concomitant use of certain anaesthetic medicines, tricyclic antidepressants and antipsychotics with ACE inhibitors may result in further reduction of blood pressure (see section 4.4).
- Sympathomimetics - Sympathomimetics may reduce the antihypertensive effects of ACE inhibitors.
- Antidiabetics - Epidemiological studies have suggested that concomitant administration of ACE inhibitors and antidiabetic medicines (insulins and oral hypoglycaemic agents) may cause an increased blood glucose lowering effect with risk of hypoglycaemia. This phenomenon appeared to be more likely to occur during the first weeks of combined treatment and in patients with renal impairment.
- Tissue Plasminogen Activators - Concomitant treatment with tissue plasminogen activators may increase the risk of angioedema.
- Acetylsalicylic acid, thrombolytics, beta-blockers, nitrates - LIZRO may be used concomitantly with acetylsalicylic acid (at cardiologic doses), thrombolytics, beta-blockers and/or nitrates.
- mTOR inhibitors (e.g. sirolimus, everolimus and temsirolimus) - Patients taking concomitant mTOR inhibitors therapy may be at increased risk for angioedema (see section 4.4).
- Co-trimoxazole (trimethoprim/sulfamethoxazole) - Patients taking concomitant co-trimoxazole (trimethoprim/sulfamethoxazole) may be at increased risk for hyperkalaemia (see section 4.4).
- Concomitant use of fluoroquinolones and ACE inhibitors as contained in LIZRO may precipitate acute kidney injury (AKI) (see section 4.3). Vulnerable patients (e.g. elderly, patients with impaired renal function, patients taking diuretics, NSAIDs and dehydrated patients) have an additional risk of nephrotoxicity.

4.6 Fertility, pregnancy and lactation
Women of childbearing potential/Contraception in males and females
Patients planning pregnancy should be changed to alternative anti-hypertensive treatments which have an established safety profile for use in pregnancy. When pregnancy is diagnosed, treatment with LIZRO should be stopped immediately and if appropriate, alternative therapy should be started.

Pregnancy
The use of LIZRO is contraindicated during pregnancy.
Pregnant women should be informed of the potential hazards to the foetus and must not take LIZRO during pregnancy (see section 4.3).
LIZRO passes through the placenta and can be presumed to cause disturbance in foetal blood pressure regulatory mechanisms. Oligohydramnios as well as hypotension, oliguria and anuria, renal failure and hyperkalaemia in newborns, have been reported after administration of LIZRO in the second and third trimester. Oligohydramnios may result in pulmonary hypoplasia and limb contractures. Cases of defective skull ossification have been observed. Prematurity and low birth mass can occur. In addition, use of LIZRO 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 (microcephaly spina bifida) and of kidney malformations. (See sections 4.3 and 4.4)
Infants who have been exposed *in utero* to LIZRO should be closely monitored. Peritoneal dialysis may be of some benefit in the clearance of LIZRO from the neonatal circulation.

Breastfeeding
Safety in lactation has not been established, and therefore mothers on LIZRO should not breastfeed their babies. (See sections 4.3 and 4.4).

4.7 Effect on ability to drive and use machines
Caution is advised when driving or performing tasks requiring alertness because of possible dizziness.

4.8 Undesirable effects

MedDRA SOC	Frequency	Description
Blood and the lymphatic system disorders	*Less frequent*	Decreases in white blood cell count (leucopenia), haemoglobin and haematocrit, bone marrow depression, anaemia, thrombocytopenia, agranulocytosis, neutropenia, lymphadenopathy, autoimmune disease, haemolytic anaemia
Endocrine disorders	*Less frequent*	Syndrome of inappropriate antidiuretic hormone secretion (SIADH), hyperkalaemia
	Unknown frequency	Hyponatraemia, increases in blood urea, increases in serum creatinine
Metabolism and nutrition disorders	*Less frequent*	Hypoglycaemia
Cardiac disorders	*Frequent*	Orthostatic effects including hypotension
	Less frequent	Myocardial infarction, cerebrovascular accident, possibly secondary to excessive hypotension in high risk patients (see section 4.4), palpitations, tachycardia
Vascular disorders	*Less frequent*	Raynaud’s phenomenon
Psychiatric disorders	*Less frequent*	Mood alterations, hallucinations, mental confusion
	Unknown frequency	Depressive symptoms
Nervous system disorders	*Frequent*	Dizziness, headache, fatigue
	Less frequent	Paraesthesia, vertigo, sleep disturbances, olfactory disturbance
	Unknown frequency	Syncope
Respiratory, thoracic and mediastinal disorders	*Frequent*	Cough
	Less frequent	Bronchospasm, rhinitis, sinusitis, allergic alveolitis/eosinophilic pneumonia
Gastrointestinal disorders	*Frequent*	Diarrhoea, nausea, vomiting
	Less frequent	Abdominal pain, indigestion, dry mouth, pancreatitis, taste disturbances, intestinal angioedema
Hepato-biliary disorders	*Less frequent*	Hepatitis (hepatocellular or cholestatic), jaundice, hepatic failure, increases in liver enzymes, increases in serum bilirubin
Skin and subcutaneous tissue disorders	*Less frequent*	Rash, urticaria, diaphoresis, alopecia, pruritus, psoriasis, severe skin disorders including pemphigus, toxic epidermal necrolysis, Stevens - Johnson syndrome and erythema multiforme, cutaneous pseudolymphoma, hypersensitivity / angioneurotic oedema: angioneurotic oedema of the face, extremities, lips, tongue, glottis, and/or larynx (see section 4.4)
	Unknown frequency	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 and connective tissue disorders	*Unknown frequency*	Asthenia
Renal and urinary disorders	*Frequent*	Renal dysfunction
	Less frequent	Uraemia, acute renal failure, oliguria/anuria
Reproductive system and breast disorders	*Less frequent*	Impotence, gynaecomastia

Safety data from clinical studies suggest that lisinopril is generally well tolerated in hypertensive paediatric patients, and that the safety profile in this age group is comparable to that seen in adults.

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 asked to report any suspected adverse reactions to SAHPRA via the “**6.04 Adverse Drug Reaction Reporting Form**”, found online under SAHPRA’s publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose
(See sections 4.4 and 4.8).

Symptoms of overdose:
Severe hypotension, electrolyte disturbances and renal failure.

Treatment of overdose:
Treatment is symptomatic and supportive. Activated charcoal may be given in severe overdosage if the patient presents within 1 hour of ingestion. Treatment consists of volume expansion to correct hypotension and treating dehydration and electrolyte imbalances. LIZRO is removable by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties:
Pharmacotherapeutic group: ACE inhibitors, plain; ATC code: C09A A04

Lisinopril inhibits angiotensin I-converting enzyme (ACE) activity. It inhibits the conversion of the relatively inactive angiotensin I to the active angiotensin II. Angiotensin II is a potent vasoconstrictor and stimulates the release of aldosterone. Decreased angiotensin II levels result in a decrease in vasopressor activity and a reduction in aldosterone secretion, which may result in small increases in serum potassium. It is also thought that ACE inhibition may inhibit degradation of bradykinin, leading to increased bradykinin levels.

5.2 Pharmacokinetic properties:

Absorption
The extent of absorption after oral administration is 25 % with wide variability between patients (6 to 60 %). The plasma half-life is 12 hours, which is increased in renal impairment. The time to achieve peak serum concentration is 7 hours. Lisinopril absorption is not affected by the presence of food.

Distribution
Lisinopril does not appear to be bound to serum proteins other than to circulating angiotensin converting enzyme (ACE). Studies in rats indicate that lisinopril crosses the blood-brain barrier poorly.

Elimination
Lisinopril is renally eliminated and excreted 100 % unchanged in the urine.

Hepatic impairment
Impairment of hepatic function in cirrhotic patients resulted in a decrease in lisinopril absorption (about 30 % as determined by urinary recovery) but an increase in exposure (approximately 50 %) compared to healthy subjects due to decreased clearance.

Renal impairment
Impaired renal function decreases elimination of lisinopril, which is excreted via the kidneys, but this decrease becomes clinically important only when the glomerular filtration rate is below 30 ml/min. In mild to moderate renal impairment (creatinine clearance 30-80 ml/min) mean AUC was increased by 13 % only, while a 4,5-fold increase in mean AUC was observed in severe renal impairment (creatinine clearance 5-30 ml/min).

Lisinopril can be removed by dialysis. During 4 hours of haemodialysis, plasma lisinopril concentrations decreased on average by 60 %, with a dialysis clearance between 40 and 55 ml/min.

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

Paediatric population
The pharmacokinetic profile of lisinopril was studied in 29 paediatric hypertensive patients, aged between 6 and 16 years, with a GFR above 30 ml/min/1,73m². After doses of 0,1 to 0,2 mg/kg, steady state peak plasma concentrations of lisinopril occurred within 6 hours, and the extent of absorption based on urinary recovery was about 28 %. These values are similar to those obtained previously in adults. AUC and C_{max} values in children in this study were consistent with those observed in adults.

Elderly
Older patients have higher blood levels and higher values for the area under the plasma concentration time curve (increased approximately 60 %) compared with younger subjects.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Calcium Hydrogen Phosphate, Anhydrous
Ferric Oxide red
Maize Starch
Magnesium stearate
Mannitol
Starch, pregelatinised

6.2 Incompatibilities
Not applicable

6.3 Shelf life
3 years

6.4 Special precautions for storage
Store at or below 30 °C. Protect from moisture.

6.5 Nature and contents of container
LIZRO 5 mg: 28’s & 30’s
30’s pack (3 blisters of 10 tablets each):
Tablets are packed in Clear 250 microns PVC coated with 60 gsm PVdC (width 178 mm) and 25 microns printed Aluminium foil (width 174 mm). Each blister contains 10 tablets.
28’s pack (2 blisters of 14 tablets each):
Tablets are packed in Clear 250 microns PVC coated with 60 gsm PVdC (width 136 mm) and 25 microns printed Aluminium foil (width 136 mm). Each blister contains 14 tablets.

LIZRO 10 mg: 28’s & 30’s
30’s pack (3 blisters of 10 tablets each):
Tablets are packed in Clear 250 microns PVC coated with 60 gsm PVdC (width 178 mm) and 25 microns printed Aluminium foil (width 174 mm). Each blister contains 10 tablets.
28’s pack (2 blisters of 14 tablets each):
Tablets are packed in Clear 250 microns PVC coated with 60 gsm PVdC (width 136 mm) and 25 microns printed Aluminium foil (width 136 mm). Each blister contains 14 tablets.

LIZRO 20 mg: 28’s & 30’s
30’s pack (3 blisters of 10 tablets each):
Tablets are packed in Clear 250 microns PVC coated with 60 gsm PVdC (width 207 mm) and 25 microns printed Aluminium foil (width 203 mm). Each blister contains 10 tablets.
28’s pack (2 blisters of 14 tablets each):
Tablets are packed in Clear 250 microns PVC coated with 60 gsm PVdC (width 248 mm) and 25 microns printed Aluminium foil (width 242 mm). Each blister contains 14 tablets.

6.6 Special precautions for disposal of a used medicine or waste materials derived from such medicine and other handling of the product
Any unused medicines and waste materials should be disposed of in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION
Novagen Pharma (Pty) Ltd
Office 2, 100 Sovereign Drive
Route 21 Corporate Park
Nellmapius Drive
Irene – Pretoria
South Africa

8. REGISTRATION NUMBER(S)
LIZRO 5 mg:
SOUTH AFRICA: A40/7.1.3/0722
NAMIBIA: 07/7.1.3/0162
LIZRO 10 mg:
SOUTH AFRICA: A40/7.1.3/0723
NAMIBIA: 07/7.1.3/0157
LIZRO 20 mg:
SOUTH AFRICA: A40/7.1.3/0724
NAMIBIA: 07/7.1.3/0163

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
Date of latest approved text: 02 February 2015.

10. DATE OF REVISION OF THE TEXT
Date of latest approved revision of text by SAHPRA: 03 April 2020.

PATIENT INFORMATION LEAFLET
SCHEDULING STATUS:
SOUTH AFRICA: S3
NAMIBIA: NS2

LIZRO 5 mg, LIZRO 10 mg LIZRO 20 mg (Tablets)

Lisinopril dihydrate

Read all of this leaflet carefully before you start taking LIZRO
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- LIZRO 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 LIZRO is and what it is used for
2. What you need to know before you take LIZRO
3. How to take LIZRO
4. Possible side effects
5. How to store LIZRO
6. Contents of the pack and other information

1. What LIZRO is and what it is used for
LIZRO is used for the treatment of:
- Mild to moderate hypertension – alone or in combination with other antihypertensives.
- Congestive heart failure – as adjunctive therapy with diuretics and where appropriate, digitalis.
- Acute myocardial infarction – LIZRO administered with 24 hours to haemodynamically stable patients reduces the risk of left ventricular dysfunction or heart failure.

2. What you need to know before you take LIZRO
Do not take LIZRO:
- If you are sensitive to lisinopril or to any of the components of LIZRO.
- If you have a history of angioedema related to previous ACE-inhibitor therapy or angiotensin receptor blockers. You should never take these medicines again.
- If you suffer from hereditary or idiopathic angioedema.
- If you suffer from aortic stenosis.
- If you suffer from hypertrophic obstructive cardiomyopathy.
- If you suffer from moderate to severe kidney function impairment (creatinine clearance below 30 ml/min).
- If you suffer from kidney artery stenosis of both kidneys.
- If you suffer from kidney artery stenosis with a single kidney.
- If you are using spironolactone, triamterene, amiloride.
- If you suffer from porphyria.
- If you are using thiazide diuretics and have Addison’s disease you should not take LIZRO in combination with thiazide diuretics. This therapy is also contraindicated in patients with severe renal impairment or anuria, and in patients who show hypersensitivity to other sulphonamide-derived medicines.
- If you are using lithium. Concomitant use of lithium with LIZRO may lead to toxic blood concentrations of lithium.
- If you are pregnant or breastfeeding.
- If you are treated with a blood pressure lowering medicine containing aliskiren.
- If you are treated with fluoroquinolone antibiotics and especially when you have moderate to severe renal impairment.

Warnings and precautions
Take special care with LIZRO:
If you are contemplating pregnancy. LIZRO should not be used during pregnancy or breastfeeding. Your doctor will prescribe you a different class of medicine if you are planning to fall pregnant.
LIZRO should be used with caution in the following conditions:
- Heart disease.
- Volume depleted patients (e.g. diuretic therapy, dietary salt restriction, dialysis, diarrhoea or vomiting).
- If you are taking any of the following medicines used to treat high blood pressure:
  − an “angiotensin II receptor blocker” (ARB) (also known as sartans - for example valsartan, telmisartan, irbesartan, etc.), in particular if you have diabetes-related kidney problems
  − aliskiren.
- Patient at a high risk of symptomatic hypotension e.g. patients with salt or volume depletion with or without hyponatremia should have these conditions corrected before therapy with LIZRO. Monitoring is required after initiating therapy.
- If you are going to have an operation (including dental surgery) tell the doctor or dentist that you are taking LIZRO. This is because you can get low blood pressure (hypotension) if you are given certain local or general anaesthetics while you are taking LIZRO.
- Severe autoimmune disease, especially systemic lupus erythematosus, other collagen vascular disease or scleroderma: Increase the risk for development of neutropenia or agranulocytosis.
- In acute myocardial infarction (heart attack), treatment with LIZRO should not be initiated in patients with evidence of kidney dysfunction. If kidney dysfunction develops during treatment, then LIZRO may need to be withdrawn.
- In acute myocardial infarction (heart attack), patients may develop persistent low blood pressure and/or impaired kidney function.
- Bone marrow depression – Increased risk of agranulocytosis and neutropenia.
- Diabetes mellitus – Increased risk of hyperkalaemia, as well as hypoglycaemia may occur.
- Hyperkalaemia – LIZRO may cause an increase in serum potassium levels.
- Kidney problems/diseases.
- If you are taking any of the following medicines, the risk of angioedema (rapid swelling under the skin in area such as the throat) is increased
  - sirolimus, everolimus and other medicines belonging to the class of mTOR inhibitors (used to avoid rejection of transplanted organs).
- Anaphylactoid reactions have occurred in patients using ACE inhibitors during desensitising protocols involving for example, hymenoptera venom.
- Anaphylactoid reactions have been reported in patients exposed to either high-flux membrane dialysis or low-density lipoprotein apheresis with dextran sulphate absorption.
- Hypersensitivity/Angioedema – If angioedema of the face, extremities, lips, tongue, glottis and/or larynx is observed in patients treated with LIZRO, LIZRO should be discontinued promptly.
- 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. These patients should never receive any LIZRO again.
- LIZRO causes a higher rate of angioedema in black patients than in non-black patients.
- Porphyria: do not use.
- Safety and efficacy in children has not been established.
- Concomitant therapy with potassium sparing diuretics such as spironolactone, triamterene, amiloride may lead to hyperkalaemia, which may be severe and lead to cardiac conduction abnormalities, dysrhythmias and cardiac arrest and should therefore not be used concomitantly.
- Cough - if you develop a dry cough which is persistent for a long time after starting treatment with LIZRO, talk to your doctor.
- If your eyes and skin become yellow (jaundice) or you have increased liver enzymes, talk to your doctor.
- If you have to take fluoroquinolone antibiotics together with LIZRO, it can cause acute kidney injury especially if you have kidney problems or you are elderly.

Children
Do not take LIZRO if you are a child.

Other medicines and LIZRO
Always tell your healthcare professional if you are taking any other medicine. (This includes complementary or traditional medicines.)
In particular, tell your doctor or pharmacist if you are taking any of the following medicines:
- An angiotensin II receptor blocker (ARB) or aliskiren, (see also information under the headings “Do not take LIZRO” and “Warnings and precautions”).
- Other medicines to help lower your blood pressure.
- Alcohol.
- Diuretics (water tablets e.g. spironolactone, triamterene or amiloride).
- Indomethacin (Non-steroidal anti-inflammatory drugs (NSAIDs) used to treat pain and arthritis).
- Potassium supplements or salt substitutes containing potassium, diuretics (water tablets, in particular those so-called potassium sparing), other medicines which can increase potassium in your body (such as heparin and co-trimoxazole also known as trimethoprim/sulfamethoxazole).
- Medicines for depression and for mental problems, including lithium.
- Medicines that contain gold, such as sodium aurothiomalate, which may be given to you as an injection.
- Medicines to treat nose or sinus congestion or other cold remedies (including those you can buy in the pharmacy).
- Insulin or medicines that you take by mouth for diabetes.
- Aspirin (Acetylsalicylic acid) if you are taking more than 3 grams each day.
- Medicines which are most often used to avoid rejection of transplanted organs (sirolimus, everolimus and other medicines belonging to the class of mTOR inhibitors).
- Concomitant use of LIZRO and fluoroquinolone antibiotics may cause your kidneys to stop working suddenly (this interaction is more likely if you are elderly, if your kidney function is impaired, you are using medicine such as water tablets, anti-inflammatory medicine or if you are dehydrated).

The following medicines may increase the risk of angioedema (signs of angioedema include swelling of the face, lips, tongue and/or throat with difficulty in swallowing or breathing):
- Medicines to break up blood clots (tissue plasminogen activator), usually given in hospital.
- See section 2 “Warnings and precautions”.

Taking LIZRO with food, drink and alcohol
LIZRO tablets may be taken with/without meals preferably at the same time every day. Alcohol may also lower your blood pressure.

Pregnancy, breastfeeding and fertility
Safety during pregnancy and lactation has not been established.
If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking LIZRO.

Driving and using machines
LIZRO can cause dizziness.
It is not always possible to predict to what extent LIZRO may interfere with your daily activities. You should ensure that you do not engage in driving a vehicle or use machines until you are aware of the measure to which LIZRO affects you.

Important information about some of the ingredients of LIZRO
LIZRO contains mannitol.

3. How to take LIZRO
Do not share medicines prescribed for you with any other person.
Always take LIZRO exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure. If you have the impression that the effect of LIZRO is too strong or too weak, talk to your doctor or pharmacist.

May be taken with/without meals preferably at the same time every day.

Mild to moderate hypertension:
Adults: Initial dose is 10 mg per day given as a single dose. The dose should be adjusted according to blood pressure response. The usual effective maintenance dose is 20 mg per day, given as a single dose with a maximum of 40 mg per day.
The full therapeutic effect may take several weeks. Therefore, if the desired effect has not been achieved within 2 to 4 weeks the dose may be increased.

Congestive heart failure:
Adults: Initial dose is 2,5 mg per day as a single dose. This may be increased at intervals of 4 weeks until the therapeutic effect is reached. Adjustments should be based on clinical response. Maintenance dosing range is 5 mg to 20 mg per day administered as a single dose.

Acute myocardial infarction:
Adults: 5 mg within 24 hours of the onset of an acute myocardial infarction, followed by 5 mg after 24 hours of the first dose, 10 mg after 48 hours of the first dose and then 10 mg per day for six weeks.
In patients with low systolic blood pressure (less than or equal to 120 mmHg), an initial dose of 2,5 mg should be used during the first three days after the infarction. If hypotension occurs (systolic blood pressure less than or equal to 100 mmHg), a daily maintenance dose of 5 mg may be given with temporary reductions of 2,5 mg if needed. If prolonged hypotension occurs (systolic blood pressure less than 90 mmHg for more than 1 hour) LIZRO should be withdrawn.
LIZRO is compatible with intravenous or transdermal glyceryl trinitrate.

Dosing in high risk individuals:
Diuretic-treated patients: In order to minimise the possibility of sudden and severe hypotension which may occur within the first 1 to 5 hours after the initial dose of LIZRO, diuretics should be discontinued 2 to 3 days before beginning therapy with LIZRO. In patients where diuretic therapy cannot be discontinued, treatment with LIZRO should be initiated with a 5 mg dose. Subsequent dosage adjustments will depend on the therapeutic response. If required, diuretic therapy may be resumed.
Renal impairment: A lower dose is required. If creatinine clearance is 31 ml - 70 ml/min the starting dose is 5 mg to 10 mg per day. The dose may be increased as needed according to therapeutic response to a maximum of 20 mg per day.
Renovascular hypertension: Dose should be lowered to 2,5 mg or 5 mg and the patient should be monitored.

LIZRO is not affected by the presence of food. LIZRO should be administered as a single daily dose at approximately the same time every day.

If you take more LIZRO than you should
Symptoms of overdose: Severe hypotension, electrolyte disturbances and renal failure.
Treatment of overdose: Please consult your doctor or pharmacist.
In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

If you forget to take LIZRO
Do not take a double dose to make up for forgotten individual doses.

If you stop taking LIZRO
As the treatment with LIZRO is usually life-long, you should discuss with your doctor before stopping LIZRO.

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

If any of the following happens, stop taking LIZRO and tell your doctor immediately or go to the casualty department at your nearest hospital:
- swelling of the hands, feet, ankles, face, lips and 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 reaction to LIZRO. 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:
- severe skin disorders, like a sudden, unexpected rash or burning, red or peeling skin
- an infection with symptoms such as fever and serious deterioration of your general condition, or fever with local infection symptoms such as sore throat/pharynx/mouth or urinary problems
- yellowing of the skin or the whites of the eyes (jaundice)
- inflammation of the liver and this can cause loss of appetite, yellowing of the skin and eyes, as well as dark coloured urine

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
- feeling dizzy or light-headed, especially if you stand up quickly
- dizziness, headache, tiredness
- cough
- diarrhoea, nausea, vomiting
- kidney problems (shown in a blood test)

Less frequent side effects
- blood disorders: decreased white blood cells, decreased haemoglobin, haematocrit, enlarged lymph nodes, breakdown of red blood cells, low blood platelet count
- passing less water (urine) than normal or passing no water
- high potassium levels in the blood
- low levels of sugar in your blood (hypoglycaemia)
- heart attack, stroke, fast heart beat
- change of colour in your fingers or toes (pale blue followed by redness)
- mood changes, feeling confused, hallucinations
- spinning feeling (vertigo), numbness or tingling in your fingers or toes
- sleep disturbances, sensory disturbances
- wheezing, sinusitis, lung disease
- stomach pain, indigestion, dry mouth, inflammation of the pancreas, taste disturbances
- intestinal angioedema with symptoms such as diffuse abdominal pain, cramping, nausea, and emesis
- liver failure, increased liver enzymes
- hives, psoriasis (a skin problem), sweating, hair loss
- a skin disease in which watery blisters form on the skin, skin eruption characterised by a typical target lesion
- increased levels of urea in the blood, kidney failure
- being unable to get an erection (impotence)
- breast enlargement in men

Side effects with unknown frequency
- low levels of sodium in your blood (the symptoms may be tiredness, headache, nausea, vomiting)
- changes in blood tests that show how well your liver and kidneys are working
- depressive symptoms
- changes to some of the cells or other parts of your blood. Your doctor may take blood samples from time to time to check whether LIZRO has had any effect on your blood. The signs may include feeling tired, pale skin, a sore throat, high temperature (fever), joint and muscle pains, swelling of the joints or glands, or sensitivity to sunlight
- lack of energy

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. This includes any possible side effects not listed in this leaflet. You can also report side effects to SAHPRA via the “**6.04 Adverse Drug Reaction Reporting Form**”, found online under SAHPRA’s publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store LIZRO
Store at or below 30 °C. Protect from moisture.
STORE ALL MEDICINES OUT OF THE REACH OF CHILDREN.
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 LIZRO contains
The active substance is lisinopril dihydrate.
LIZRO 5 mg: Each tablet contains 5,44 mg lisinopril dihydrate equivalent to anhydrous lisinopril 5 mg.
LIZRO 10 mg: Each tablet contains 10,87 mg lisinopril dihydrate equivalent to anhydrous lisinopril 10 mg.
LIZRO 20 mg: Each tablet contains 21,74 mg lisinopril dihydrate equivalent to anhydrous lisinopril 20 mg.
The other ingredients are calcium hydrogen phosphate anhydrous; ferric oxide red, magnesium stearate; maize starch; mannitol and starch pregelatinised.

LIZRO contains sugar (i.e. mannitol).

What LIZRO looks like and contents of the pack
LIZRO 5 mg:
Light red coloured, round shaped, biconvex, uncoated tablets, debossed with ‘L’ on one side and on other side with ‘5’ on one side of the score line.
LIZRO 10 mg:
Light yellow coloured, round shaped, biconvex, uncoated tablets, debossed with ‘L’ on one side and on other side with ‘10’.
LIZRO 20 mg:
Light yellow coloured, capsule shaped, biconvex, uncoated tablets, debossed with ‘L’ on one side and on other side with ‘20’.

LIZRO 5 mg: 28’s & 30’s
1. 30’s pack (3 blisters of 10 tablets each):
Tablets are packed in Clear 250 microns PVC coated with 60 gsm PVdC (width 178 mm) and 25 microns printed Aluminium foil (width 174 mm). Each blister contains 10 tablets.
2. 28’s pack (2 blisters of 14 tablets each):
Tablets are packed in Clear 250 microns PVC coated with 60 gsm PVdC (width 136 mm) and 25 microns printed Aluminium foil (width 136 mm). Each blister contains 14 tablets.

LIZRO 10 mg: 28’s & 30’s
1. 30’s pack (3 blisters of 10 tablets each):
Tablets are packed in Clear 250 microns PVC coated with 60 gsm PVdC (width 178 mm) and 25 microns printed Aluminium foil (width 174 mm). Each blister contains 10 tablets.
2. 28’s pack (2 blisters of 14 tablets each):
Tablets are packed in Clear 250 microns PVC coated with 60 gsm PVdC (width 136 mm) and 25 microns printed Aluminium foil (width 136 mm). Each blister contains 14 tablets.

LIZRO 20 mg: 28’s & 30’s
1. 30’s pack (3 blisters of 10 tablets each):
Tablets are packed in Clear 250 microns PVC coated with 60 gsm PVdC (width 207 mm) and 25 microns printed Aluminium foil (width 203 mm). Each blister contains 10 tablets.
2. 28’s pack (2 blisters of 14 tablets each):
Tablets are packed in Clear 250 microns PVC coated with 60 gsm PVdC (width 248 mm) and 25 microns printed Aluminium foil (width 242 mm). Each blister contains 14 tablets.

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NAMIBIA: 07/7.1.3/0162
LIZRO 10 mg:
SOUTH AFRICA: A40/7.1.3/0723
NAMIBIA: 07/7.1.3/0157
LIZRO 20 mg:
SOUTH AFRICA: A40/7.1.3/0724
NAMIBIA: 07/7.1.3/0163

PROFESSIONELE INLIGTING

NOVAGEN PHARMA

SKEDULERINGSTATUS
SUID-AFRIKA: S3
NAMIBIË: NS2

1. NAAM VAN DIE MEDISYNE
LIZRO 5 mg (Tablette)
LIZRO 10 mg (Tablette)
LIZRO 20 mg (Tablette)

2. KWALITATIEWE EN KWANTITATIEWE SAMESTELLING
LIZRO 5 mg: Elke tablet bevat 5,44 mg lisinoprieldihidraat gelykstaande aan anhidriese lisinopriel 5 mg.
LIZRO 10 mg: Elke tablet bevat 10,87 mg lisinoprieldihidraat gelykstaande aan anhidriese lisinopriel 10 mg.
LIZRO 20 mg: Elke tablet bevat 21,74 mg lisinoprieldihidraat gelykstaande aan anhidriese lisinopriel 20 mg.

LIZRO bevat suiker (dit wil sê mannitol).

Vir die volledige lys hulpstowwe sien afdeling 6.1 .

3. FARMASEUTIESE VORM
Tablette

LIZRO 5 mg: Ligrooikleurige, ronde, bikonvekse, onbedekte tablette, met 'L' aan die een kant gedruk en aan die ander kant met '5' gedruk aan die een kant van die breeklyn.
LIZRO 10 mg: Liggeelkleurige, ronde, bikonvekse, onbedekte tablette, met 'L' aan die een kant en '10' aan die ander kant gedruk.
LIZRO 20 mg: Liggeelkleurige, kapsuulvormige, bikonvekse, onbedekte tablette, met 'L' aan die een kant en '20'aan die ander kant gedruk.

4. KLINIESE BESONDERHEDE

4.1 Terapeutiese indikasies
LIZRO word aangedui vir die behandeling van:
- Ligte tot matige hipertensie - alleen of in kombinasie met ander anti-hipertensiewe middels.
- Kongestiewe hartversaking - as aanvullende terapie met diuretika en waar toepaslik, digitalis.
- Akute miokardiale infarksie - LIZRO wat binne 24 uur aan hemodinamies stabiele pasiënte toegedien word, verminder die risiko van linkerventrikulêre disfunksie of hartversaking.

4.2 Posologie en metode van toediening
Kan met/sonder maaltye geneem word, verkieslik op dieselfde tyd elke dag.

Ligte tot Matige hipertensie:
Volwassenes: Die aanvanklike dosis is 10 mg per dag as 'n enkel dosis. Die dosis moet volgens die bloeddrukrespons aangepas word. Die gewone effektiewe onderhoudsdosis is 20 mg per dag, gegee as 'n enkel dosis met 'n maksimum van 40 mg per dag.
Die volledige terapeutiese effek kan 'n paar weke duur. Dus, as die gewenste effek nie binne 2 tot 4 weke bereik is nie, kan die dosis verhoog word.

Kongestiewe hartversaking:
Volwassenes: Die aanvanklike dosis is 2,5 mg per dag as 'n enkel dosis. Dit kan met tussenposes van 4 weke verhoog word totdat die terapeutiese effek bereik word. Aanpassings moet gebaseer wees op kliniese respons. Die doseringsomvang vir onderhoud is 5 mg tot 20 mg per dag toegedien as 'n enkel dosis.

Akute Miokardiale Infarksie:
Volwassenes: 5 mg binne 24 uur na die begin van 'n akute miokardiale infarksie, gevolg deur 5 mg na 24 uur van die eerste dosis, 10 mg na 48 uur van die eerste dosis en daarna 10 mg per dag vir ses weke. By pasiënte met 'n lae sistoliese bloeddruk (minder as of gelyk aan 120 mmHg), moet 'n aanvanklike dosis van 2,5 mg gedurende die eerste drie dae na die infarksie gebruik word. Indien hipotensie voorkom (sistoliese bloeddruk kleiner as of gelyk aan 100 mmHg), kan 'n daaglikse onderhoudsdosis van 5 mg gegee word met tydelike verlaging van 2,5 mg indien nodig. Indien langdurige hipotensie voorkom (sistoliese bloeddruk minder as 90 mmHg vir langer as 1 uur), moet LIZRO onttrek word.

Dosering by individue met 'n hoë risiko:
Pasiënte wat diureties behandel is: Om die moontlikheid van skielike en ernstige hipotensie te verminder, wat binne die eerste 1 tot 5 uur na die aanvanklike dosis LIZRO kan voorkom, moet die diuretika gestaak word 2 tot 3 dae voordat die behandeling met LIZRO begin. By pasiënte waar diuretiese behandeling nie gestaak kan word nie, moet die behandeling met LIZRO met 'n dosis van 5 mg begin word. Daaropvolgende doseringsaanpassings sal afhang van die terapeutiese respons. Indien nodig, kan diuretiese terapie hervat word.

Nierinkorting: 'n Laer dosis is nodig. Indien kreatinienopruiming 31 ml - 70 ml/min is, is die aanvangsdosis 5 mg tot 10 mg per dag. Die dosis kan volgens die terapeutiese respons tot 20 mg per dag verhoog word soos nodig.

Renovaskulêre hipertensie: Die dosis moet verlaag word tot 2,5 mg of 5 mg en die pasiënt moet gemoniteer word.
LIZRO word nie deur die teenwoordigheid van voedsel beïnvloed nie. LIZRO moet elke dag as 'n enkel dosis toegedien word, ongeveer dieselfde tyd.

4.3 Kontraïndikasies
- Gevoeligheid vir enige van die komponente van LIZRO.
- 'n Geskiedenis van angio-edeem wat verband hou met vorige terapie met AOE-remmers of angiotensienreseptorblokkeerders (ARB's): Hierdie pasiënte moet nooit weer hierdie medisyne kry nie.
- Oorerflike of idiopatiese angio-edeem.
- Aortastenose.
- Hipertrofiese obstruktiewe kardiomiopatie (HOKM).
- Matige tot ernstige verswakte nierfunksie (kreatinienopruiming minder as 30 ml/min).
- Bilaterale renale arteriële stenose.
- Renale arteriële stenose by pasiënte met 'n enkele nier.
- Gelyktydige behandeling met kaliumsparende diuretika soos spironolaktoon, triamtereen en amiloried.
- Porfirie.
- Tiasied-diuretika in (vaste dosis) kombinasie met LIZRO moet nie gegee word aan pasiënte met Addison se siekte nie. Hierdie terapie is ook teenaangedui by pasiënte met ernstige nierfunksie of anurie, en by pasiënte wat hipersensitiwiteit toon vir ander sulfonamied-afgeleide medisyne.
- Litiumterapie: Gelyktydige toediening met LIZRO kan lei tot toksiese bloedkonsentrasies van litium.
- Swangerskap en laktasie (sien afdeling 4.4 en 4.6)
- Die gelyktydige gebruik van LIZRO saam met aliskiren-bevattende produkte is teenaangedui.
- Gelyktydige gebruik van fluorokinolone en AOE-remmers soos bevat in LIZRO, is teenaangedui by pasiënte met matige tot ernstige nierfunksie.

4.4 Spesiale waarskuwings en voorsorgmaatreëls vir gebruik

As 'n vrou swanger raak terwyl sy LIZRO ontvang, moet die behandeling onmiddellik gestaak word en na 'n ander klas medisyne oorgeskakel word. (Sien afdeling 4.3 en 4.6). Indien 'n vrou swangerskap oorweeg, moet 'n ander klas medisyne gebruik word. (Sien afdeling 4.3 en 4.6).

LIZRO moet met omsigtigheid gebruik word by die volgende kondisies:
- Serebrovaskulêre siekte of iskemiese hartsiektes - Vermindering in bloeddruk kan hierdie toestande vererger en kan lei tot miokardiale infarksie en serebrovaskulêre ongelukke.
- Volume-uitgeputte pasiënte (bv. deur diuretiese terapie, soutbeperking in die dieet, dialise, diarree of braking). Alhoewel dit by normo-volumiese pasiënte kan voorkom, is hipotensie meer waarskynlik by pasiënte met volume-uitputting. 'n Skielike afname in angiotensien II kan lei tot 'n skielike en ernstige hipotensie. Daar is ook 'n verhoogde risiko vir nierversaking deur LIZRO, veral by diegene met kongestiewe hartversaking. By pasiënte met volume-uitputting of pasiënte met iskemiese hartsiektes of serebrovaskulêre siektes, moet terapie gemonitor word, veral as die dosis LIZRO of diuretikum aangepas word.
- Daar is bewyse dat die gelyktydige gebruik van AOE-remmers, angiotensien II-reseptorblokkeerders (ARB's) of aliskirien die risiko van hipotensie, hiperkalemie kan verhoog en die nierfunksie kan verminder (insluitend akute nierversaking). Dubbele blokkering van RAAS deur die gekombineerde gebruik van LIZRO en aliskiren word dus teenaangedui (sien afdeling 4.3).
- Pasiënte met 'n hoë risiko vir simptomatiese hipotensie, bv. pasiënte met sout- of volume-uitputting met of sonder hiponatremie moet hierdie toestande laat regstel voor behandeling met LIZRO. Monitering is nodig na die aanvang van terapie. Indien hipotensie voorkom, moet die pasiënt in die rugposisie geplaas word en indien nodig 'n intraveneuse infusie van 0,9 % soutoplossing ontvang.
- By pasiënte wat 'n groot operasie ondergaan of tydens verdowing met medisyne wat hipotensie voortbring, kan LIZRO die vorming van angiotensien II sekondêr tot komplementêre renienvrystelling blokkeer. Indien hipotensie voorkom en as gevolg van hierdie meganisme beskou word, kan dit deur volume-uitbreiding reggestel word.
- Ernstige outo-immuun siekte, veral sistemiese lupus erythematosus, ander kollageen vaskulêre siekte of sklerodermie: Verhoog die risiko vir ontwikkeling van neutropenie of agranulositose.
- By akute miokardiale infarksie, moet behandeling met LIZRO nie begin word by pasiënte met bewyse van nierdisfunksie nie (serumkreatinienkonsentrasies van meer as 177 mikromol/L of proteïnurie van meer as 500 mg/24 uur). Indien nierdisfunksie ontwikkel tydens behandeling (serumkreatinienkonsentrasies van meer as 177 mikromol/L of verdubbeling van die voorbehandelingswaarde), kan LIZRO moontlik onttrek word.
- By akute miokardiale infarksie kan pasiënte aanhoudende hipotensie en/of verswakte nierfunksie ontwikkel.
- Hipotensie by akute miokardiale infarksie - Behandeling met LIZRO moet nie begin word by pasiënte met akute miokardiale infarksie wat die risiko het van 'n verdere ernstige hemodinamiese agteruitgang na behandeling met 'n vasodilator nie. Dit sluit in pasiënte met 'n sistoliese bloeddruk van 100 mmHg of laer of kardiogeniese skok. Gedurende die eerste 3 dae na die infarksie moet die dosis verminder word as die sistoliese bloeddruk 120 mmHg of laer is. Onderhoudsdosisse moet verminder word tot 5 mg of tydelik tot 2,5 mg as sistoliese bloeddruk 100 mmHg of laer is. Indien hipotensie voortduur (sistoliese bloeddruk minder as 90 mmHg vir langer as 1 uur), moet LIZRO onttrek word.
- Beenmurgonderdrukking - Verhoogde risiko vir agranulositose en neutropenie.
- Diabetes mellitus - Verhoogde risiko vir hiperkalemie, sowel as hipoglisemie, kan voorkom.
- Hiperkalemie - LIZRO kan 'n toename in serumkaliumvlakke veroorsaak.
- Renovaskulêre siekte - LIZRO moet nie gebruik word by pasiënte met 'n renovaskulêre siekte of 'n vermoedelike renovaskulêre siekte nie, maar dit kan versigtig gebruik word by ernstige weerstandige hipertensie by sulke pasiënte. In hierdie geval moet LIZRO slegs onder spesialis toesig gebruik word. Bejaarde pasiënte met perifere vaskulêre siektes of veralgemeende aterosklerose kan asimptomatiese renovaskulêre siektes hê. (Sien afdeling 4.2).
- Renale arteriële stenose, bilateraal of in een nier- of nieroorplanting - 'n Verhoogde risiko vir verswakking van die nierfunksie kan verhoogde ureum en serumkreatinien konsentrasies in die bloed veroorsaak, wat omkeerbaar kan wees as die behandeling gestaak word. Daar is ook 'n verhoogde risiko vir agranulositose en neutropenie wanneer immuunonderdrukkers gelyktydig toegedien word.
- Nierfunksie verswakking - Verminderde eliminasie van LIZRO wat lei tot 'n verhoogde risiko vir hiperkalemie. Hierdie pasiënte kan laer dosisse benodig.
- Toename in ureum en serumkreatinien in die bloed is waargeneem by pasiënte met geen voorafbestaande vaskulêre siekte nie, veral as LIZRO tesame met 'n diuretikum toegedien is. Doseringsvermindering of staking van LIZRO of die diuretikum kan nodig wees.
- Gelyktydige gebruik van mTOR-remmers (bv. sirolimus, everolimus en temsirolimus): Pasiënte wat gelyktydig mTOR-remmers (bv. sirolimus, everolimus en temsirolimus) terapie gebruik, kan 'n groter risiko hê vir angio-edeem (bv. swelling van die lugweë of tong, met of sonder verswakking van asemhaling)) (sien afdeling 4.5).
- Anafilaktoïede reaksies het voorgekom by pasiënte wat AOE-remmers gebruik tydens desensiterende protokolle wat onder meer hymenoptera gif insluit.
- Anafilaktoïede reaksies is gerapporteer by pasiënte wat blootgestel is aan óf hoëvloeistofmembraandialise of lae-digtheid lipoproteïn-aferese met dekstraansulfaatabsorpsie.
- Hipersensitiwiteit/Angio-edeem - Indien angio-edeem van die gesig, ledemate, lippe, tong, glottis en/of larinks by pasiënte wat met LIZRO behandel word, waargeneem word, moet LIZRO onmiddellik gestaak word. Hierdie pasiënte moet gemonitor word om volledige oplossing van die simptome te verseker.
- Angioedeem wat verband hou met laringeale edeem kan fataal wees. Waar daar 'n betrokkenheid van die tong, glottis of larinks is, wat moontlik lugwegbelemmering kan veroorsaak, moet toepaslike noodterapie toegedien word. Dit kan insluit die toediening van adrenalien en/of die instandhouding van 'n patente lugweg. Die pasiënt moet onder noukeurige mediese toesig wees totdat die simptome volledig en volgehou opgelos is. **Hierdie pasiënte moet nooit weer enige LIZRO ontvang nie.**
- LIZRO veroorsaak 'n hoër persentasie van angio-edeem by swart pasiënte as by nie-swart pasiënte.
- Porfirie: teenaangedui (sien afdeling 4.3).
- Veiligheid en effektiwiteit by kinders is nie vasgestel nie.
- Gelyktydige behandeling met kaliumsparende diuretika soos spironolaktoon, triamtereen en amiloried kan lei tot hiperkalemie, wat ernstig kan wees en kan lei tot abnormaliteite in die hartgeleiding, disritmieë en hartstilstand en is daarom teenaangedui (sien afdeling 4.3).
- Hoes: Hoes is aangemeld met die gebruik van AOE-remmers soos bevat in LIZRO. Kenmerkend, is die hoes nie-produktief, aanhoudend en los op nadat die behandeling gestaak is. AOE-remmer- geïnduseerde hoes moet beskou word as deel van die differensiële diagnose van hoes.
- AOE-remmers, soos vervat in LIZRO, word baie selde geassosieer met 'n sindroom wat begin met cholestatiese geelsug en vorder tot fulminante nekrose en (soms) dood. Die meganisme van hierdie sindroom word nie verstaan nie. Pasiënte wat LIZRO ontvang, wat geelsug of duidelike toename in die lewerensieme ontwikkel, moet LIZRO stop en toepaslike mediese opvolg behandeling kry.
- Gelyktydige gebruik van fluorokinoloon-antibiotika en AOE-remmers (soos bevat in LIZRO) kan akute nierbeserings veroorsaak by pasiënte, veral dié met matige tot ernstige ingekorte nierfunksie en bejaarde pasiënte. (sien afdeling 4.3). Die nierfunksie moet beoordeel word voor die behandeling met fluorokinolone of AOE-remmers begin word, en moet tydens die behandeling gemonitor word,.

4.5 Interaksie met ander medisyne en ander vorme van interaksie
Gelyktydige gebruik van LIZRO saam met:
- ARB's, AOE-remmers of aliskiren - Kliniese proefdata het aangetoon dat dubbele blokkade van die renien-angiotensien-aldosteroon-stelsel (RAAS) deur die gekombineerde gebruik van AOE-remmers, angiotensien II-reseptorblokkeerders of aliskirien geassosieer word met 'n hoër frekwensie van newe-effekte soos hipotensie, hiperkalemie en verminderde nierfunksie (sien afdelings 4.3 en 4.4).
- Diuretika, alkohol en hipotensie-produserende medikasie - Die anti-hipertensiewe effek is toevoegend. Doseringsaanpassings kan nodig wees tydens gelyktydige gebruik of wanneer een medisyne gestaak word.
- Lus, tiasied of verwante diuretika - "Eerste dosis hipotensie" kan voorkom (Sien afdeling 4.2).
- Indometasien en nie-steroïedale anti-inflammatoriese medisyne (NSAIM's) - verminder die anti-hipertensiewe effekte van LIZRO. Bloeddrukmonitering moet verhoog word wanneer enige NSAIM bygevoeg of gestaak word by 'n pasiënt wat met LIZRO behandel word.
- Kaliumaanvullings of kaliumsparende diuretika soos spironolaktoon, triamtereen of amiloried - gelyktydige toediening kan lei tot hiperkalemie.
- Litium - Daar is 'n toename in litiumkonsentrasies gerapporteer. Gereelde monitering van serum-litiumkonsentrasies word aanbeveel.
- Goud - Nitritoïedreaksies (simptome van vasodilatasie insluitend gloede, naarheid, duiseligheid en hipotensie, wat baie ernstig kan wees) is na aanleiding van inspuitbare goud (byvoorbeeld natriumaurothiomalaat) meer gereeld gerapporteer by pasiënte wat AOE-remmerterapie ontvang.
- Trisikliese antidepressante/Antipsigotika/Verdowingsmiddels - Gelyktydige gebruik van sekere verdowingsmiddels, trisikliese antidepressante en antipsigotika met AOE-remmers kan lei tot verdere verlaging van die bloeddruk (sien afdeling 4.4).
- Simpatomimetika - Simpatomimetika kan die anti-hipertensiewe effekte van AOE-remmers verminder.
- Antidiabetika - Epidemiologiese studies het voorgestel dat gelyktydige toediening van AOE-remmers en antidiabetiese medisyne (insulien en orale hipoglukemiese middels) 'n verhoogde bloedglukoseverlagende effek kan veroorsaak met die risiko van hipoglukemie. Dit lyk asof hierdie verskynsel meer waarskynlik is om voor te kom gedurende die eerste weke van die gekombineerde behandeling en by pasiënte met ingeperkte nierfunksie.
- Weefselplasminogeen-aktiveerders - Gelyktydige behandeling met weefselplasminogeen-aktiveerders kan die risiko van angio-edeem verhoog.
- Asetielsalisielsuur, trombolitiese middels, beta-blokkers, nitrate - LIZRO kan gelyktydig met asetielsalisielsuur gebruik word (teen kardiologiese dosisse), trombolitiese middels, beta-blokkers en/of nitrate.
- mTOR-remmers (bv. sirolimus, everolimus en temsirolimus) - Pasiënte wat gelyktydig mTOR-remmers behandeling gebruik, kan 'n groter risiko vir angio-edeem hê (sien afdeling 4.4).
- Ko-trimoksasool (trimetopriem/sulfamethoksasool) - Pasiënte wat gelyktydig ko-trimoksasool (trimetopriem/sulfamethoksasool) neem, kan 'n groter risiko vir hiperkalemie hê (sien afdeling 4.4).
- Gelyktydige gebruik van fluorokinolone en AOE-remmers soos bevat in LIZRO, kan akute nierbeserings (AKI) veroorsaak (sien afdeling 4.3). Kwesbare pasiënte (bv. bejaardes, pasiënte met verswakte nierfunksie, pasiënte wat diuretika neem, NSAIM's en ontwaterde pasiënte) het 'n addisionele risiko vir nefrotoksisiteit.

4.6 Vrugbaarheid, swangerskap en laktasie
Vroue van swangerskap potensiaal/Voorbehoeding by mans en vrouens
Pasiënte wat swangerskap beplan, moet verander word na alternatiewe anti-hipertensiewe behandelings wat 'n gevestigde veiligheidsprofiel het vir gebruik tydens swangerskap. Wanneer swangerskap gediagnoseer word, moet die behandeling met LIZRO onmiddellik gestaak word en indien toepaslik, moet alternatiewe behandeling begin word.

Swangerskap
Die gebruik van LIZRO is teenaangedui tydens swangerskap.
Swanger vroue moet ingelig word oor die moontlike gevare vir die fetus en moet nie LIZRO tydens swangerskap gebruik nie (sien afdeling 4.3).
LIZRO kruis die plasenta en daar word vermoed dat dit versteuring in die reguleringsmeganismes van fetale bloeddruk veroorsaak. Na toediening van LIZRO in die tweede en derde trimester is oligohidramnios sowel as hipotensie, oligurie en anurie, nierversaking en hiperkalemie by pasgeborenes aangemeld. Oligohidramnios kan pulmonale hipoplasie en ledemaatkontrakture tot gevolg hê. Gevalle van gebrekkige ossifikasie van die skedel is waargeneem. Premature en lae geboortemassa kan voorkom. Daarbenewens het die gebruik van LIZRO gedurende die eerste trimester van swangerskap gepaard gegaan met 'n verhoogde risiko van geboortedefekte, veral die kardiovaskulêre en die sentrale senuweestelsel ("microcephaly spina bifida") en van niermisvormings. (Sien afdelings 4.3 en 4.4)
Babas wat *in-utero* blootgestel is aan LIZRO, moet fyn dopgehou word. Peritoneale dialise kan tot sommige voordeel strek by die opruiming van LIZRO uit die neonatale sirkulasie.

Borsvoeding
Veiligheid tydens laktasie is nie vasgestel nie, en moeders op LIZRO moenie hul babas borsvoed nie. (Sien afdelings 4.3 en 4.4).

4.7 Effek op die vermoë om te bestuur en masjiene te gebruik
Wees versigtig as u bestuur of take uitvoer wat waaksaamheid vereis as gevolg van moontlike duiseligheid.

4.8 Ongewenste effekte

MedDRA SOK	Frekwensie	Beskrywing
Bloed- en limfstelsel-afwykings	*Minder gereeld*	Afname in witbloedseltelling (leukopenie), hemoglobien en hematokrit, beenmurgonderdrukking, bloedarmoede, trombositopenie, agranulositose, neutropenie, limfadenopatie, outo-immuun siekte, hemolitiese anemie
Endokriene afwykings	*Minder gereeld*	Sindroom van ontoepaslike antidiuretiese hormoonafskeiding (SIADH), hiperkalemie
	Onbekende frekwensie	Hiponatremie, toename in bloedureum, toename in serumkreatinien
Metabolisme- en voedingsafwykings	*Minder gereeld*	Hipoglisemie
Hartafwykings	*Gereeld*	Ortostatiese effekte insluitend hipotensie
	Minder gereeld	Miokardiale infarksie, serebrovaskulêre ongeluk, moontlik sekondêr tot oormatige hipotensie by pasiënte met 'n hoë risiko (sien afdeling 4.4), hartkloppings, tagikardie
Vaskulêre afwykings	*Minder gereeld*	Raynaud se verskynsel
Psigiatriese afwykings	*Minder gereeld*	Gemoedsveranderinge, hallusinasies, geestelike verwarring
	Onbekende frekwensie	Depressiewe simptome
Senuweestelselafwykings	*Gereeld*	Duiseligheid, hoofpyn, moegheid
	Minder gereeld	Parestesie, vertigo, slaapsteurnisse, reukversteuring
	Onbekende frekwensie	Sinkopee
Respiratoriese-, torakale en mediastinale afwykings	*Gereeld*	Hoes
	Minder gereeld	Brongospasme, rinitis, sinusitis, allergiese alveolitis/eosinofiliese longontsteking
Gastroïntestinale afwykings	*Gereeld*	Diarree, naarheid, braking
	Minder gereeld	Abdominale pyn, slegte spysvertering, droë mond, pankreatitis, smaakversteuringe, intestinale angio-edeem
Hepato-biliêre afwykings	*Minder gereeld*	Hepatitis (hepatosellulêre of cholestatiese), geelsug, lewerversaking, verhogings in lewerensieme, verhogings in serum bilirubien
Vel- en subkutane weefselafwykings	*Minder gereeld*	Uitslag, urtikarie, diaphorese, alopesie, pruritus, psoriase, ernstige velafwykings insluitend pempigus, toksiese epidermale nekrolise, Stevens - Johnson sindroom en erythema multiforme, kutane pseudolimfoma, hipersensitiwiteit/angioneurotiese edeem: angioneurotiese edeem van die gesig, ledemate, lippe, tong, glottis, en/of larinks (sien afdeling 4.4)
	Onbekende frekwensie	Daar is 'n simptoomkompleks aangemeld wat een of meer van die volgende kan insluit: koors, vaskulitis, mialgie, artralgie/artritis, 'n positiewe antinukleêre teenliggaampie (ANA), verhoogde rooibloedselle sedimentasietempo (ESR), eosinofilie en leukositose, uitslag, fotosensitiwiteit of ander dermatologiese manifestasies kan voorkom.
Muskuloskeletale- en bindweefselafwykings	*Onbekende frekwensie*	Astenie
Renale en urinêre afwykings	*Gereeld*	Renale disfunksie
	Minder gereeld	Uremie, akute nierversaking, oligurie/anurie
Reproduktiewe sisteem en borsafwykings	*Minder gereeld*	Impotensie, ginekomastie

Veiligheidsdata uit kliniese studies dui daarop dat lisinopriel in die algemeen goed verdra word by hipertensiewe pediatriese pasiënte, en dat die veiligheidsprofiel in hierdie ouderdomsgroep vergelykbaar is met dié wat by volwassenes gesien word.

Rapportering van vermoedelike newe-reaksies
Dit is belangrik om vermoedelike newe-reaksies na die goedkeuring van die medisyne te rapporteer. Dit laat die voortgesette monitering van die voordeel/risiko-balans van die medisyne toe. Professionele gesondheidsorgpersoneel word versoek om enige vermoedelike newe-reaksies by SAHPRA aan te meld via die "**6.04 Adverse Drug Reaction Reporting Form**" wat aanlyn gevind word onder SAHPRA se publikasies: https://www.sahpra.org.za/Publications/Index/8.

4.9 Oordosis
(Sien afdelings 4.4 en 4.8).

Simptome van oordosis:
Erge hipotensie, elektrolietversteurings en nierversaking.

Behandeling van oordosis:
Behandeling is simptomaties en ondersteunend. As die pasiënt binne 1 uur na inname opdaag, kan geaktiveerde houtskool by ernstige oordosering toegedien word. Behandeling bestaan uit volume-uitbreiding om hipotensie te korrigeer en dehidrasie en elektrolietwanbalanse te behandel. LIZRO kan deur hemodialise verwyder word.

5. FARMAKOLOGIESE EIENSKAPPE

5.1 Farmakodinamiese eienskappe:
Farmakoterapeutiese groep: AOE-remmers, gewoon; ATC-kode: C09A A04

Lisinopriel inhibeer die aktiwiteit van angiotensien I-omskakelingsensiem (AOE). Dit belemmer die omskakeling van die relatief onaktiewe angiotensien I na die aktiewe angiotensien II. Angiotensien II is 'n kragtige vasokonstriktor en stimuleer die vrystelling van aldosteroon. Verlaagde angiotensien II-vlakke lei tot 'n afname in vasopressor-aktiwiteit en 'n afname in aldosteroon-afskeiding, wat tot 'n klein toename in serumkalium kan lei. Daar word ook gedink dat AOE-remming die agteruitgang van bradikinien kan belemmer, wat tot verhoogde bradikinienvlakke lei.

5.2 Farmakokinetiese eienskappe:

Absorpsie
Die omvang van absorpsie na orale toediening is 25 %, met groot variasie tussen pasiënte (6 tot 60 %). Die plasma-halfleeftyd is 12 uur, wat verhoog is by nierinkorting. Die tyd om die piek in serum te bereik is 7 uur. Die opname van lisinopriel word nie beïnvloed deur die teenwoordigheid van voedsel nie.

Verspreiding
Dit lyk nie asof lisinopriel aan ander serumproteïene gebonde is nie, maar aan angiotensienomskakelende ensiem (AOE). Studies by rotte dui daarop dat lisinopriel die bloed-breinskans swak kruis.

Eliminasie
Lisinopriel word renaal geëlimineer en 100 % onveranderd in die urine uitgeskei.

Lewerinkorting
Verswakking van lewerfunksie by sirrotiese pasiënte het gelei tot 'n afname in absorpsie van lisinopriel (ongeveer 30 % soos bepaal deur urinêre herwinning), maar 'n toename in blootstelling (ongeveer 50 %) in vergelyking met gesonde persone as gevolg van verminderde opruiming.

Nierinkorting
Swak nierfunksie verminder die eliminasie van lisinopriel wat via die niere uitgeskei word, maar hierdie afname word klinies belangrik slegs as die glomerulêre filtrasietempo onder 30 ml/min is. By ligte tot matige nierinkorting (kreatinienopruiming 30-80 ml/min) is die gemiddelde AOK slegs met 13 % verhoog, terwyl 'n 4,5-voudige toename in die gemiddelde AOK waargeneem is by ernstige nierinkorting (kreatinienopruiming 5-30 ml/min).

Lisinopriel kan deur dialise verwyder word. Gedurende 4 uur van hemodialise het die plasmakonsentrasies van lisinopriel gemiddeld met 60 % gedaal, met 'n dialise-opruiming tussen 40 en 55 ml/min.

Hartversaking
Pasiënte met hartversaking het 'n groter blootstelling aan lisinopriel in vergelyking met gesonde proefpersone ('n toename in AOK gemiddeld van 125 %), maar gebaseer op die urinêre herstel van lisinopriel is daar 'n verminderde absorpsie van ongeveer 16 % in vergelyking met gesonde persone.

Pediatriese bevolking
Die farmakokinetiese profiel van lisinopriel is bestudeer by 29 pediatriese hipertensiewe pasiënte, tussen 6 en 16 jaar oud, met 'n GFR hoër as 30 ml/min/1,73 m². Na dosisse van 0,1 tot 0,2 mg/kg, het die vastevlak piek-plasmakonsentrasies van lisinopriel binne 6 uur plaasgevind, en die mate van absorpsie gebaseer op urine herwinning was ongeveer 28 %. Hierdie waardes is soortgelyk aan dié wat voorheen by volwassenes verkry is. Die AOK- en K_{maks}-waardes by kinders in hierdie studie stem ooreen met dié wat by volwassenes waargeneem is.

Bejaardes
Ouer pasiënte het hoër bloedvlakke en hoër waardes vir die area onder die plasma-konsentrasietydkurwe (verhoog ongeveer 60 %) in vergelyking met jonger persone.

6. FARMASEUTIESE BESONDERHEDE

6.1 Lys van hulpstowwe
Kalsiumwaterstoffosfaat, Anhidries
Ysteroksied rooi
Mieliestysel
Magnesiumstearaat
Mannitol
Stysel, vooraf-gegelatiniseerd

6.2 Onversoenbaarhede
Nie van toepassing nie

6.3 Rakleeftyd
3 jaar

6.4 Spesiale voorsorgmaatreëls vir bewaring
Bewaar teen of benede 30 °C. Beskerm teen vog.

6.5 Aard en inhoud van die houer
LIZRO 5 mg: 28's en 30's
30's-pak (3 stolpstroke van 10 tablette elk):
Tablette word verpak in helder 250 mikron PVC-bedek met 60 gsm PVdC (breedte 178 mm) en 25 mikron gedrukte Aluminiumfoelie (breedte 174 mm). Elke stolpstrook bevat 10 tablette.
28's-pak (2 stolpstroke van 14 tablette elk):
Tablette word verpak in helder 250 mikron PVC bedek met 60 gsm PVdC (breedte 136 mm) en 25 mikron gedrukte Aluminiumfoelie (breedte 136 mm). Elke stolpstrook bevat 14 tablette.

LIZRO 10 mg: 28's & 30's
30's-pak (3 stolpstroke van 10 tablette elk):
Tablette word verpak in helder 250 mikron PVC-bedek met 60 gsm PVdC (breedte 178 mm) en 25 mikron gedrukte Aluminiumfoelie (breedte 174 mm). Elke stolpstrook bevat 10 tablette.
28's-pak (2 stolpstroke van 14 tablette elk):
Tablette word verpak in helder 250 mikron PVC bedek met 60 gsm PVdC (breedte 136 mm) en 25 mikron gedrukte Aluminiumfoelie (breedte 136 mm). Elke stolpstrook bevat 14 tablette.

LIZRO 20 mg: 28's en 30's
30's-pak (3 stolpstroke van 10 tablette elk):
Tablette word verpak in helder 250 mikron PVC-bedek met 60 gsm PVdC (breedte 207 mm) en 25 mikron gedrukte Aluminiumfoelie (breedte 203 mm). Elke stolpstrook bevat 10 tablette.
28's-pak (2 stolpstroke van 14 tablette elk):
Tablette word verpak in helder 250 mikron PVC bedek met 60 gsm PVdC (breedte 248 mm) en 25 mikron gedrukte Aluminiumfoelie (breedte 242 mm). Elke stolpstrook bevat 14 tablette.

6.6 Spesiale voorsorgmaatreëls vir die wegdoen van 'n gebruikte medisyne of afvalstowwe afkomstig van die medisyne en ander hantering van die produk
Ongebruikte medisyne en afvalstowwe moet weggedoen word volgens die plaaslike vereistes.

7. HOUER VAN DIE SERTIFIKAAT VAN REGISTRASIE
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Kantoor 2, Sovereignrylaan 100
Route 21 Corporate Park
Nellmapiusrylaan
Irene - Pretoria
Suid-Afrika

8. REGISTRASIENOMMER(S)
LIZRO 5 mg:
SUID-AFRIKA: A40/7.1.3/0722
NAMIBIË: 07/7.1.3/0162
LIZRO 10 mg:
SUID-AFRIKA: A40/7.1.3/0723
NAMIBIË: 07/7.1.3/0157
LIZRO 20 mg:
SUID-AFRIKA: A40/7.1.3/0724
NAMIBIË: 07/7.1.3/0163

9. DATUM VAN EERSTE MAGTIGING/HERNUWING VAN DIE MAGTIGING
Datum van die nuutste goedgekeurde teks: 02 Februarie 2015.

10. DATUM VAN HERSIENING VAN DIE TEKS
Datum van die nuutste goedgekeurde hersiening van teks deur SAHPRA: 03 April 2020.

P1525214

PASIËNTINLIGTINGBILJET
SKEDULERINGSTATUS:
SUID-AFRIKA: S3
NAMIBIA: NS2

LIZRO 5 mg, LIZRO 10 mg LIZRO 20 mg (Tablette)

Lisinoprieldihidraat

Lees die hele pamflet sorgvuldig deur voordat u LIZRO begin neem
- Bewaar hierdie pamflet. Miskien moet u dit weer lees.
- As u enige verdere vrae het, vra asseblief u dokter of apteker.
- LIZRO is vir u persoonlik voorgeskryf en u moet nie u medisyne met ander mense deel nie. Dit kan hulle benadeel, selfs al is hul simptome dieselfde as joune.

Wat is in hierdie pamflet
1. Wat is LIZRO en waarvoor word dit gebruik
2. Wat u moet weet voordat u LIZRO neem
3. Hoe om LIZRO te neem
4. Moontlike newe-effekte
5. Hoe u LIZRO bêre
6. Inhoud van die verpakking en ander inligting

1. Wat is LIZRO en waarvoor word dit gebruik?
LIZRO word gebruik vir die behandeling van:
- Ligte tot matige hipertensie - alleen of in kombinasie met ander anti-hipertensiewe middels.
- Kongestiewe hartversaking - as aanvullende terapie met diuretika en waar toepaslik, digitalis.
- Akute miokardiale infarksie - LIZRO wat 24 uur aan hemodinamies stabiele pasiënte toegedien word, verminder die risiko van linkerventrikulêre disfunksie of hartversaking.

2. Wat u moet weet voordat u LIZRO neem
Moenie LIZRO neem nie:
- As u sensitief is vir lisinopriel of vir enige van die bestanddele van LIZRO.
- As u 'n geskiedenis van angio-edeem het wat verband hou met vorige AOE-remmerterapie of angiotensienreseptor-blokkers. U mag hierdie medisyne nooit weer neem nie.
- As u aan oorerflike of idiopatiese angio-edeem ly.
- As u aan aortastenose ly.
- As u aan hipertrofiese obstruktiewe kardiomiopatie ly.
- As u aan matige tot ernstige verswakte nierfunksie ly (kreatinienopruiming onder 30 ml/min).
- As u ly aan nier arteriële stenose van beide niere.
- As u ly aan nier arteriële stenose met 'n enkele nier.
- As u spironolaktoon, triamtereen, of amiloried gebruik.
- As u aan porfirie ly.
- As u tiasied-diuretika gebruik en Addison se siekte het, moet u nie LIZRO in kombinasie met tiasied-diuretika neem nie. Hierdie terapie is ook teenaangedui by pasiënte met ernstige nierverswakking of anurie, en by pasiënte wat hipersensitiwiteit toon vir ander medisyne afgelei van sulfonamied.
- As u litium gebruik. Gelyktydige gebruik van litium en LIZRO kan lei tot toksiese bloedkonsentrasies van litium.
- As u swanger is of borsvoed.
- As u behandel word met 'n bloeddrukverlagende medisyne wat aliskirien bevat.
- As u behandel word met fluorokinoloon-antibiotika en veral as u matig tot ernstige verswakte nierfunksie het.

Waarskuwings en voorsorgmaatreëls
Wees veral versigtig met LIZRO:
As u swangerskap oorweeg. LIZRO moet nie tydens swangerskap of borsvoeding gebruik word nie. U dokter sal vir u 'n ander klas medisyne voorskryf as u van plan is om swanger te raak.
LIZRO moet met versigtigheid gebruik word by die volgende kondisies:
- Hartsiekte.
- Volume-uitgeputte pasiënte (bv. diuretiese terapie, soutbeperking in die dieet, dialise, diarree of braking).
- As u een van die volgende medisyne neem wat gebruik word om hoë bloeddruk te behandel:
  - 'n "angiotensien II-reseptorblokker" (ARB's) (ook bekend as sartans - byvoorbeeld valsartan, telmisartan, irbesartan, ens.), veral as u suikersiekte-verwante nierprobleme het.
  - aliskirien.
- Pasiënt met 'n hoë risiko vir simptomatiese hipotensie, bv. pasiënte met sout- of volume-uitputting met of sonder hiponatremie moet hierdie toestande laat regstel voor behandeling met LIZRO. Monitering is nodig nadat die terapie begin is.
- As u 'n operasie (insluitend tandheelkundige chirurgie) gaan ondergaan, vertel die dokter of tandarts dat u LIZRO neem. Dit is omdat u lae bloeddruk (hipotensie) kan kry as u sekere lokale of algemene verdowingsmiddels kry terwyl u LIZRO neem.
- Ernstige outo-immuun siekte, veral sistemiese lupus erythematosus, ander kollageen vaskulêre siekte of sklerodermie: Verhoog die risiko vir die ontwikkeling van neutropenie of agranulositose.
- By akute miokardiale infarksie (hartaanval), moet behandeling met LIZRO nie begin word by pasiënte met bewyse van nierdisfunksie nie. As nierdisfunksie tydens behandeling ontwikkel, kan LIZRO moontlik teruggetrek word.
- By akute miokardiale infarksie (hartaanval), kan pasiënte aanhoudende lae bloeddruk en/of verswakte nierfunksie ontwikkel.
- Beenmurgonderdrukking - Verhoogde risiko vir agranulositose en neutropenie.
- Diabetes mellitus - Verhoogde risiko vir hiperkalemie, sowel as hipoglisemie, kan voorkom.
- Hiperkalemie - LIZRO kan 'n toename in kaliumvlakke in serum veroorsaak.
- Nierprobleme/siektes.
- As u een van die volgende medisyne neem, word die risiko vir angio-edeem (vinnige swelling onder die vel in areas soos die keel) verhoog.
  - sirolimus, everolimus en ander medisyne wat tot die klas mTOR-remmers behoort (gebruik om verwerping van oorgeplante organe te vermy).
- Anafilaktoïede reaksies het voorgekom by pasiënte wat AOE-remmers gebruik tydens desensitiserende protokolle wat onder meer hymenoptera gif insluit.
- Anafilaktoïede reaksies is gerapporteer by pasiënte wat blootgestel is aan óf hoëvloeistofmembraandialise of 'n lae-digtheid lipoproteïn-aferese met dekstraansulfaatabsorpsie.
- Hipersensitiwiteit/Angio-edeem - As angio-edeem van die gesig, ledemate, lippe, tong, glottis en/of larinks by pasiënte wat met LIZRO behandel word, waargeneem word, moet LIZRO onmiddellik gestaak word.
- Angio-edeem wat verband hou met laringeale edeem kan fataal wees. Waar daar 'n betrokkenheid van die tong, glottis of larinks is, wat moontlik lugwegbelemmering kan veroorsaak, moet toepaslike noodterapie toegedien word. Hierdie pasiënte moet nooit weer enige LIZRO ontvang nie.
- LIZRO veroorsaak 'n hoër persentasie angio-edeem by swart pasiënte as by nie-swart pasiënte.
- Porfirie: Moenie gebruik nie.
- Veiligheid en effektiwiteit by kinders is nie vasgestel nie.
- Gelyktydige behandeling met kaliumsparende diuretika soos spironolaktoon, triamtereen, amiloried kan lei tot hiperkalemie, wat ernstig kan wees en kan lei tot abnormaliteite in die hartgeleiding, disritmieë en hartstilstand en moet daarom nie gelyktydig gebruik word nie.
- Hoes - praat met u dokter as u 'n droë hoes ontwikkel wat aanhoudend is vir 'n lang tyd nadat u met LIZRO begin het.
- As u oë en vel geel word (geelsug) of u lewerensieme vermeerder het, praat met u dokter.
- As u fluorokinoloon-antibiotika saam met LIZRO moet neem, kan dit akute nierbeserings veroorsaak, veral as u nierprobleme het of bejaard is.

Kinders
Moenie LIZRO neem as u kind is nie.

Ander medisyne en LIZRO
Vertel altyd u gesondheidsorgwerker as u enige ander medisyne neem. (Dit sluit komplementêre of tradisionele medisyne in.)
Vertel veral u dokter of apteker as u een van die volgende medisyne neem:
- 'n Angiotensien II-reseptorblokker (ARB) of aliskirien, (sien ook inligting onder die opskrifte "Moenie LIZRO neem nie" en "Waarskuwings en voorsorgmaatreëls").
- Ander medisyne om u bloeddruk te help verlaag.
- Alkohol.
- Diuretika (watertablette, bv. spironolaktoon, triamtereen of amiloried).
- Indometasien (Nie-steroïedale anti-inflammatoriese middels (NSAIM's) wat gebruik word om pyn en artritis te behandel).
- Kaliumaanvullings of soutvervangers wat kalium bevat, diuretika (watertablette, veral die sogenaamde kaliumsparende), ander medisyne wat kalium in u liggaam kan verhoog (soos heparien en ko-trimoksasool, ook bekend as trimetopriem/sulfametoksasool).
- Medisyne vir depressie en vir geestelike probleme, insluitend litium.
- Medisyne wat goud bevat, soos natriumurothiomalaat, wat as 'n inspuiting aan u gegee kan word.
- Medisyne om kongestie in die neus of sinus te behandel, of ander verkouemedisyne (insluitend medisyne wat u in die apteek kan koop).
- Insulien of medisyne wat u per mond neem vir diabetes.
- Aspirien (Asetielsalisielsuur) as u elke dag meer as 3 gram inneem.
- Medisyne wat meestal gebruik word om verwerping van oorgeplante organe te vermy (sirolimus, everolimus en ander medisyne wat tot die klas mTOR-remmers behoort).
- Gelyktydige gebruik van LIZRO en fluorokinoloon antibiotika kan daartoe lei dat u niere skielik ophou werk (hierdie interaksie is meer waarskynlik as u ouer is, as u nierfunksie verswak is, u medisyne gebruik soos watertablette, anti-inflammatoriese medisyne of ontwater is).

Die volgende medisyne kan die risiko van angio-edeem verhoog (tekens van angio-edeem is swelling van die gesig, lippe, tong en/of keel met probleme om te sluk of asem te haal):
- Medisyne om bloedklonte op te breek (weefselplasminogeen-aktivator), gewoonlik gegee in die hospitaal.
- Sien afdeling 2 "Waarskuwings en voorsorgmaatreëls".

Neem van LIZRO saam met voedsel, drinkgoed en alkohol
LIZRO tablette kan saam met/sonder maaltye geneem word, verkieslik op dieselfde tyd elke dag. Alkohol kan ook u bloeddruk verlaag.

Swangerskap, borsvoeding en vrugbaarheid
Veiligheid tydens swangerskap en laktasie is nie vasgestel nie.
As u swanger is of u baba borsvoed, raadpleeg asseblief u dokter, apteker of ander gesondheidsorgwerker vir advies voordat u LIZRO neem.

Bestuur en gebruik van masjiene
LIZRO kan duiseligheid veroorsaak.
Dit is nie altyd moontlik om te voorspel tot watter mate LIZRO met u daaglikse aktiwiteite kan inmeng nie. U moet seker maak dat u nie 'n voertuig bestuur of masjiene gebruik voordat u bewus is van die omvang waartoe LIZRO u affekteer nie.

Belangrike inligting oor sommige van die bestanddele van LIZRO
LIZRO bevat mannitol.

3. Hoe om LIZRO te neem
Moenie medisyne wat vir u voorgeskryf is, met enige ander persoon deel nie.
Neem altyd LIZRO presies soos deur u dokter voorgeskryf. U moet met u dokter of apteker kontak maak as u onseker is. As u die indruk het dat die effek van LIZRO te sterk of te swak is, praat dan met u dokter of apteker.

Kan met/sonder maaltye geneem word, verkieslik op dieselfde tyd elke dag.

Ligte tot matige hipertensie:
Volwassenes: Die aanvanklike dosis is 10 mg per dag as 'n enkel dosis. Die dosis moet volgens die bloeddrukrespons aangepas word. Die gewone effektiewe onderhoudsdosis is 20 mg per dag, gegee as 'n enkel dosis met 'n maksimum van 40 mg per dag.
Die volledige terapeutiese effek kan 'n paar weke duur. Daarom, as die gewenste effek nie binne 2 tot 4 weke bereik is nie, kan die dosis verhoog word.

Kongestiewe hartversaking:
Volwassenes: Die aanvanklike dosis is 2,5 mg per dag as 'n enkel dosis. Dit kan met tussenposes van 4 weke verhoog word totdat die terapeutiese effek bereik word. Aanpassings moet gebaseer wees op kliniese respons. Die doseringsomvang vir onderhoud is 5 mg tot 20 mg per dag toegedien as 'n enkel dosis.

Akute miokardiale infarksie:
Volwassenes: 5 mg binne 24 uur na die begin van 'n akute miokardiale infarksie, gevolg deur 5 mg na 24 uur van die eerste dosis, 10 mg na 48 uur van die eerste dosis en daarna 10 mg per dag vir ses weke.
By pasiënte met 'n lae sistoliese bloeddruk (minder as of gelyk aan 120 mmHg), moet 'n aanvanklike dosis van 2,5 mg gedurende die eerste drie dae na die infarksie gebruik word. As hipotensie voorkom (sistoliese bloeddruk minder as of gelyk aan 100 mmHg), kan 'n daaglikse onderhoudsdosis van 5 mg gegee word met tydelike verlaging van 2,5 mg indien nodig. As langdurige hipotensie voorkom (sistoliese bloeddruk minder as 90 mmHg vir langer as 1 uur), moet LIZRO onttrek word.
LIZRO is verenigbaar met binneaarse of transdermale gliserieltrinitraat.

Dosering by individue met 'n hoë risiko:
Pasiënte wat diureties behandel is: Om die moontlikheid van skielike en ernstige hipotensie te veminder, wat binne die eerste 1 tot 5 uur na die aanvanklike dosis LIZRO kan voorkom, moet die diuretika gestaak word 2 tot 3 dae voordat die behandeling met LIZRO begin word. By pasiënte waar diuretiese behandeling nie gestaak kan word nie, moet die behandeling met LIZRO met 'n dosis van 5 mg begin word. Daaropvolgende doseringsaanpassings sal afhang van die terapeutiese respons. Indien nodig, kan diuretiese terapie hervat word.
Verswakte nierfunksie: 'n Laer dosis is nodig. As kreatinienopruiming 31 ml - 70 ml/min is, is die aanvangsdosis 5 mg tot 10 mg per dag. Die dosis kan volgens die terapeutiese respons tot 'n maksimum van 20 mg per dag verhoog word, soos nodig.
Renovaskulêre hipertensie: Die dosis moet verlaag word tot 2,5 mg of 5 mg en die pasiënt moet gemoniteer word.

LIZRO word nie deur die teenwoordigheid van voedsel beïnvloed nie. LIZRO moet elke dag ongeveer dieselfde tyd as 'n enkel dosis toegedien word.

As u meer LIZRO neem as wat u moet
Simptome van oordosis: Erge hipotensie, elektrolietversteurings en nierversaking.
Behandeling van oordosis: Raadpleeg asseblief u dokter of apteker.
In die geval van oordosering, raadpleeg u dokter of apteker. As daar nie een beskikbaar is nie, kontak die naaste hospitaal of gifbeheersentrum.

As u vergeet om LIZRO te neem
Moet nie 'n dubbele dosis neem om vir die dosisse wat vergeet is, op te maak nie.

As u ophou om LIZRO te neem
Aangesien die behandeling met LIZRO gewoonlik lewenslank is, moet u dit met u dokter bespreek voordat u met LIZRO stop.

4. Moontlike newe-effekte
LIZRO kan newe-effekte hê.
Nie alle newe-effekte wat vir LIZRO aangemeld is, is in hierdie pamflet ingesluit nie. Raadpleeg asseblief u dokter, apteker of ander gesondheidsorgwerker vir advies indien u algemene gesondheid vererger, of as u slegte gevolge ondervind tydens die gebruik van LIZRO.

As een van die volgende gebeur, moet u ophou om LIZRO te neem en dit onmiddellik aan u dokter vertel of na die ongevalle-afdeling by u naaste hospitaal gaan:
- swelling van die hande, voete, enkels, gesig, lippe en mond of keel, wat probleme met sluk of asemhaling kan veroorsaak,
- uitslag of jeuk,
- floute.

Dit is alles baie ernstige newe-effekte. As u dit het, het u moontlik 'n ernstige reaksie op LIZRO gehad. U kan dringend mediese hulp of hospitalisasie benodig.

Vertel u dokter onmiddellik of gaan na die ongevalle-afdeling by u naaste hospitaal as u een van die volgende opmerk:
- ernstige velafwykings, soos 'n skielike, onverwagte veluitslag of brandende, rooi of afskilferende vel
- 'n infeksie met simptome soos koors en ernstige agteruitgang van u algemene toestand, of koors met plaaslike infeksiesimptome soos seer keel/farinks/mond of urinêre probleme
- vergeling van die vel of die wit van die oë (geelsug)
- inflammasie van die lewer, en dit kan verlies van eetlus, vergeling van die vel en oë, asook donkerkleurige urine veroorsaak

Dit is alles ernstige newe-effekte. U kan dringend mediese hulp benodig.

Vertel u dokter as u een van die volgende opmerk:
Gereelde newe-effekte
- voel duiselig of lighoofdig, veral as u vinnig opstaan
- duiseligheid, hoofpyn, moegheid
- hoes
- diarree, naarheid, braking
- nierprobleme (getoon in 'n bloedtoets)

Minder gereelde newe-effekte
- bloedafwykings: verminderde witbloedselle, verlaagde hemoglobien, hematokrit, vergrote limfnodes, afbreek van rooibloedselle, lae bloedplaatjie-telling
- minder water (urine) as normaal te laat gaan of geen water deurlaat nie
- hoë kaliumvlakke in die bloed
- lae suikervlakke in u bloed (hipoglukemie)
- hartaanval, beroerte, vinnige hartslag
- kleurverandering in u vingers of tone (ligblou gevolg deur rooiheid)
- gemoedsveranderinge, verwarde gevoel, hallusinasies
- spin gevoel (vertigo), gevoelloosheid of tinteling in jou vingers of tone
- slaapstoornisse, sensoriese versteurings
- hyging, sinusitis, longsiekte
- maagpyn, spysvertering, droë mond, inflammasie van die pankreas, smaakversteurings
- intestinale angio-edeem met simptome soos diffuse buikpyn, kramp, naarheid en emese
- lewerversaking, verhoogde lewerensieme
- korwe, psoriase ('n velprobleem), sweet, haarverlies
- 'n velsiekte waarin waterige blase op die vel vorm, veluitbarsting wat gekenmerk word deur 'n tipiese teiken letsel
- verhoogde vlakke van ureum in die bloed, nierversaking
- nie in staat wees om 'n ereksie te kry nie (impotensie)
- borsvergroting by mans

Newe-effekte met onbekende frekwensie
- lae natriumvlakke in u bloed (die simptome kan moegheid, hoofpyn, naarheid, braking wees)
- veranderinge in bloedtoetse wat wys hoe goed u lewer en niere werk
- depressiewe simptome
- veranderinge aan sommige van die selle of ander dele van u bloed. U dokter kan van tyd tot tyd bloedmonsters neem om te kyk of LIZRO u bloed beïnvloed het. Die tekens kan insluit moegheid, bleek vel, 'n seer keel, hoë temperatuur (koors), gewrigs- en spierpyn, swelling van die gewrigte of kliere, of sensitiwiteit vir sonlig
- gebrek aan energie

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

Rapportering van newe-effekte
Praat met u dokter, apteker of verpleegster as u newe-effekte opdoen. Dit sluit in enige moontlike newe-effekte wat nie in hierdie pamflet gelys word nie. U kan ook newe-effekte by SAHPRA aanmeld via die "**6.04 Adverse Drug Reaction Reporting Form**", wat aanlyn gevind word onder SAHPRA se publikasies: https://www.sahpra.org.za/Publications/Index/8. Deur newe-effekte aan te meld, kan u help om meer inligting oor die veiligheid van hierdie medisyne te gee.

5. Hoe om LIZRO te bêre
Berg teen of benede 30 °C. Beskerm teen vog.
BERG ALLE MEDISYNE BUITE DIE BEREIK VAN KINDERS.
Neem alle ongebruikte medisyne terug na u apteker.
Moenie ongebruikte medisyne in dreine of rioolstelsels (bv. toilette) wegdoen nie.

6. Inhoud van die verpakking en ander inligting
Wat LIZRO bevat
Die aktiewe stof is lisinoprieldihidraat.
LIZRO 5 mg: Elke tablet bevat 5,44 mg lisinoprieldihidraat gelykstaande aan 5 mg watervrye lisinopriel.
LIZRO 10 mg: Elke tablet bevat 10,87 mg lisinoprieldihidraat gelykstaande aan 10 mg watervrye lisinopriel.
LIZRO 20 mg: Elke tablet bevat 21,74 mg lisinoprieldihidraat gelykstaande aan 20 mg watervrye lisinopriel.
Die ander bestanddele is watervrye kalsiumwaterstoffosfaat; ysteroksied rooi, magnesiumstearaat; mieliestysel; mannitol en vooraf-gegelatiniseerde stysel.

LIZRO bevat suiker (dit wil sê mannitol).

Hoe LIZRO lyk en die inhoud van die verpakking
LIZRO 5 mg:
Ligrooikleurige, ronde, bikonvekse, onbedekte tablette, met 'L' aan die een kant gedruk en aan die ander kant met '5' gedruk aan die een kant van die breeklyn.
LIZRO 10 mg:
Liggeelkleurige, ronde, bikonvekse, onbedekte tablette, met 'L' aan die een kant en '10' aan die ander kant gedruk.
LIZRO 20 mg:
Liggeelkleurige, kapsuulvormige, bikonvekse, onbedekte tablette, met 'L' aan die een kant en '20' aan die ander kant gedruk.

LIZRO 5 mg: 28's en 30's
1.30's-pak (3 stolpstroke van 10 tablette elk):
Tablette word verpak in helder 250 mikron PVC-bedek met 60 gsm PVdC (breedte 178 mm) en 25 mikron gedrukte Aluminiumfoelie (breedte 174 mm). Elke stolpstrook bevat 10 tablette.
2.28's-pak (2 stolpstroke van 14 tablette elk):
Tablette word verpak in helder 250 mikron PVC bedek met 60 gsm PVdC (breedte 136 mm) en 25 mikron gedrukte Aluminiumfoelie (breedte 136 mm). Elke stolpstrook bevat 14 tablette.

LIZRO 10 mg: 28's & 30's
1.30's-pak (3 stolpstroke van 10 tablette elk):
Tablette word verpak in helder 250 mikron PVC-bedek met 60 gsm PVdC (breedte 178 mm) en 25 mikron gedrukte Aluminiumfoelie (breedte 174 mm). Elke stolpstrook bevat 10 tablette.
2.28's-pak (2 stolpstroke van 14 tablette elk):
Tablette word verpak in helder 250 mikron PVC bedek met 60 gsm PVdC (breedte 136 mm) en 25 mikron gedrukte Aluminiumfoelie (breedte 136 mm). Elke stolpstrook bevat 14 tablette.

LIZRO 20 mg: 28's en 30's
1.30's-pak (3 stolpstroke van 10 tablette elk):
Tablette word verpak in helder 250 mikron PVC-bedek met 60 gsm PVdC (breedte 207 mm) en 25 mikron gedrukte Aluminiumfoelie (breedte 203 mm). Elke stolpstrook bevat 10 tablette.
2.28's-pak (2 stolpstroke van 14 tablette elk):
Tablette word verpak in helder 250 mikron PVC bedek met 60 gsm PVdC (breedte 248 mm) en 25 mikron gedrukte Aluminiumfoelie (breedte 242 mm). Elke stolpstrook bevat 14 tablette.

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Pinkode: 500 090
INDIË

Hierdie pamflet is laas hersien in
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Registrasienommer(s)
LIZRO 5 mg:
SUID-AFRIKA: A40/7.1.3/0722
NAMIBIË: 07/7.1.3/0162
LIZRO 10 mg:
SUID-AFRIKA: A40/7.1.3/0723
NAMIBIË: 07/7.1.3/0157
LIZRO 20 mg:
SUID-AFRIKA: A40/7.1.3/0724
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