Professional Information

SCHEDULING STATUS:

S3

1. NAME OF THE MEDICINE

Enalapril Unicorn 5 (Tablets)

Enalapril Unicorn 10 (Tablets)

Enalapril Unicorn 20 (Tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Enalapril Unicorn 5

Each tablet contains

Enalapril maleate 5 mg

Contains sugar: Lactose 40 mg per tablet

Contains sodium: 0,131 mg per tablet

Enalapril Unicorn 10

Each tablet contains

Enalapril maleate 10 mg

Contains sugar: Lactose 80 mg per tablet

Contains sodium: 0,262 mg per tablet

Enalapril Unicorn 20

Each tablet contains

Enalapril maleate 20 mg

Contains sugar: Lactose 80 mg per tablet

Contains sodium: 0,262 mg per tablet

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet

Enalapril Unicorn 5

White to off-white round, biconvex uncoated tablets debossed with ‘ENP005’ and a break line on one side and ‘R’ on the other.

Enalapril Unicorn 10

Pink, round biconvex uncoated tablets debossed with ‘ENP010’ on one side and ‘R’ on the other.

Enalapril Unicorn 20

Peach coloured round, biconvex, uncoated tablets debossed with ‘ENP020’ on one side and ‘R’ on the other.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of hypertension.

Treatment of heart failure: **Enalapril Unicorn** is indicated for the treatment of symptomatic congestive heart failure, usually in combination with diuretics and digitalis. In these patients **Enalapril Unicorn** improves symptoms, increases survival, and decreases the frequency of hospitalization.

Asymptomatic left ventricular dysfunction: In clinically stable asymptomatic patients with left ventricular dysfunction (ejection fraction < 35 %), enalapril decreases the rate of development of overt heart failure and decreases the incidence of hospitalisation for heart failure.

4.2 Posology and method of administration

Posology

Since food does not interfere with the absorption of **Enalapril Unicorn**, the dose may be administered before, during or after meals.

***Essential hypertension*:** The initial dose is 10 to 20 mg depending on the degree of hypertension and is given once daily. In mild hypertension the recommended initial dose is 10 mg daily. For other degrees of hypertension the initial dose is 20 mg daily. The usual maintenance dose is one 20 mg tablet taken once daily. The dosage should be adjusted according to the needs of the patient.

***Concomitant diuretic therapy in hypertension*:** Symptomatic hypotension may occur following the initial dose of **Enalapril Unicorn**; this is more likely in patients who are being treated currently with diuretics. Caution is recommended, therefore, since these patients may be volume or salt depleted. The diuretic therapy should be discontinued for 2-3 days prior to initiation of therapy with **Enalapril Unicorn**. If this is not possible, the initial dose of enalapril should be low (5 mg or less) to determine the initial effect on the blood pressure. Dosage should then be adjusted according to the needs of the patient.

Use in the elderly (over 65 years): Therapy should be initiated with **Enalapril Unicorn** in a dose of 2,5 mg. The hypotensive response to **Enalapril Unicorn** may be greater in elderly patients.

***Heart failure/ asymptomatic left ventricular dysfunction*:** In such patients the recommended starting dose of **Enalapril Unicorn** is 2,5 mg once daily initiated under medical supervision to determine the initial effect on the blood pressure. It is important that therapy is initiated in hospital for patients with severe heart failure. The dose of **Enalapril Unicorn** should be titrated gradually to a maintenance dose of 20 mg daily given as a single dose or two divided doses, according to the tolerability of the patient.

The dose titration of **Enalapril Unicorn** should be performed over two to four weeks or more rapidly in the presence of residual signs and symptoms of heart failure. The patient's blood pressure, renal function and serum potassium must be monitored closely both before and during treatment with **Enalapril Unicorn** because hypotension and consequent renal failure have been reported.

Patients who are treated with diuretics should have the diuretic dose reduced, if possible, before starting treatment with **Enalapril Unicorn**. In case hypotension develops following the initial dose of **Enalapril Unicorn**, this does not imply that hypotension will recur during chronic therapy with **Enalapril Unicorn** and does not preclude continued use of **Enalapril Unicorn**.

Dosage in renal Insufficiency:

(See Section 4.4**,** *Impaired Renal Function*).

Generally the intervals between the administration of enalapril should be prolonged and/or the dosage reduced.

Renal status	**Creatinine Clearance (ml/min)**	**Initial Dose (mg/day)**
Mild impairment	< 80 > 50	5
Moderate impairment	< 50 > 30	2,5

Serum potassium also should be regularly monitored (see Section 4.4 and 4.5).

Method of administration

Oral use

4.3 Contraindications

- **Enalapril Unicorn** should not be used in patients with known hypersensitivity to enalapril or any of the excipients of **Enalapril Unicorn** (listed in section 6.1).
- A history of angioedema relating to previous ACE inhibitor or angiotensin receptor blockers (ARBs) treatment: Such patients must never again be given these medicines.
- Hereditary or idiopathic angioedema.
- Hypertrophic obstructive cardiomyopathy (HOCM).
- Severe renal function impairment (creatinine clearance less than 30 ml/min).

- Bilateral renal artery stenosis.
- Renal artery stenosis in patients with a single kidney.
- Aortic stenosis.
- Concomitant therapy with potassium sparing diuretics such as spironolactone, triamterene, amiloride.
- Porphyria.
- Lithium therapy: Concomitant administration with **Enalapril Unicorn** may lead to toxic blood concentrations of lithium.
- Pregnancy and lactation (see Section 4.4 and 4.6).
- The concomitant use of **Enalapril Unicorn** with aliskiren-containing products is contraindicated.
- Concomitant use of fluoroquinolones with ACE inhibitors/renin-angiotensin blockers 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 **Enalapril Unicorn**, the treatment must be stopped promptly and switched to a different class of medicine. Should a woman contemplate pregnancy, the doctor should institute alternative medication. (See Section 4.3 and 4.6).

Dual blockade of the renin-angiotensin-aldosterone system (RAAS) 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 **Enalapril Unicorn** and aliskiren is therefore

contraindicated (see Section 4.3). **Enalapril Unicorn** should not be used concomitantly with aliskiren. (see Section 4.3).

Enalapril Unicorn can cause foetal and neonatal morbidity and mortality when administered to pregnant women during the 2nd and 3rd trimesters (see Section 4.3 and 4.4).

Assessment of renal function prior to initiation of **Enalapril Unicorn** and during treatment with **Enalapril Unicorn** should be included in the evaluation of patient, where appropriate.

Symptomatic hypotension: Symptomatic hypotension can occur especially in patients who are volume-depleted e.g. by diuretic therapy, dietary salt restriction, dialysis, diarrhoea or vomiting (see Section 4.5 and 4.8). In patients with heart failure, with or without associated renal insufficiency, symptomatic hypotension is most likely to occur in those with more severe degrees of heart failure, as reflected by the use of high doses of loop diuretics, hyponatraemia or functional renal impairment (See Section 4.2 for management of these patients). In these patients, therapy should be started under medical supervision and the patient should be monitored closely whenever the dose of **Enalapril Unicorn** and/or diuretic is adjusted. Similarly, patients with ischaemic heart or cerebrovascular disease may develop an excessive fall in blood pressure which could result in a myocardial infarction or cerebrovascular accident.

If hypotension develops, suitable management including placing the patient in a supine position and, if necessary, an intravenous infusion of normal saline may be required. A transient hypotensive response is not a contra-indication to further doses, which can be given with monitoring once the blood pressure is increased after volume expansion.

Some patients with heart failure who have normal or low blood pressure could develop additional lowering of systemic blood pressure following **Enalapril Unicorn** administration. If symptomatic

hypotension occurs, a reduction of dose of **Enalapril Unicorn** and/or discontinuation of the diuretic may be necessary (see Section 4.2).

Impaired Renal Function: Caution should be exercised when using **Enalapril Unicorn** in patients with renal insufficiency. Such patients may require reduced or less frequent doses (see Section 4.2). The renal function should be monitored before and during therapy in those with renal insufficiency.

Renovascular hypertension: **Enalapril Unicorn** is contra-indicated in renovascular hypertension (see Section 4.3).

Kidney Transplantation: There is no experience regarding the administration of **Enalapril Unicorn** in patients with recent kidney transplantation. Treatment with **Enalapril Unicorn** is therefore not recommended.

Concomitant use of fluoroquinolones and ACE inhibitors/renin-angiotensin receptor blockers 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/renin-angiotensin receptor blockers.

Hepatic failure: Patients receiving **Enalapril Unicorn** who develop jaundice or marked elevations of hepatic enzymes should discontinue **Enalapril Unicorn** and receive appropriate medical follow-up.

Neutropenia/Agranulocytosis: Neutropenia/agranulocytosis, thrombocytopenia and anaemia have been reported in patients receiving ACE inhibitors including **Enalapril Unicorn**. **Enalapril Unicorn** should be used with extreme caution in patients with collagen vascular disease, immunosuppressant therapy, treatment with allopurinol or procainamide, or a combination of these complicating factors,

especially if there is pre-existing impaired renal function. Some of these patients developed serious infections which in a few instances did not respond to intensive antibiotic therapy.

Hypersensitivity/Angioneurotic oedema: Angioneurotic oedema of the face, extremities, lips, tongue, glottis and/or larynx has been seen to occur following treatment with **Enalapril Unicorn**. This may occur at any time during treatment. In such cases, **Enalapril Unicorn** should be discontinued immediately and appropriate monitoring should be taken to ensure complete resolution of symptoms prior to discharging the patient. Angioneurotic oedema associated with laryngeal oedema may be fatal. Involvement of the tongue, glottis or larynx, likely to cause airways obstruction, necessitates emergency measures such as prompt administration of subcutaneous adrenaline (0,3-0,5 ml, 1: 1000).

Black patients receiving **Enalapril Unicorn** have been reported to have a higher incidence of angioedema compared with non-black patients.

Patients with a history of angioedema unrelated to **Enalapril Unicorn** should be considered to be at increased risk of angioedema while receiving **Enalapril Unicorn** (see also Section 4.3).

Anaphylactic reactions during hymenoptera desensitisation: Patients receiving **Enalapril Unicorn** during desensitisation with hymenoptera venom (e.g. bee or wasp venom) have been found to experience life threatening hypersensitivity reactions. Temporarily withholding **Enalapril Unicorn** therapy prior to each desensitisation can help avert such reactions.

Hypersensitivity reactions during LDL apheresis: Less frequently, patients receiving ACE inhibitors during low density lipoprotein (LDL)-apheresis with dextran sulphate have experienced life-threatening hypersensitivity reactions. These reactions may be avoided by withholding **Enalapril Unicorn** therapy prior to each apheresis.

Haemodialysis patients: In patients dialysed with high-flux membranes and treated concomitantly with **Enalapril Unicorn** a high incidence of anaphylactoid reactions have been reported. It is recommended that in such patients a different type of dialysis membrane or a different class of antihypertensive agent should be used.

Hypoglycaemia: Diabetic patients treated with oral antidiabetic agents or insulin starting **Enalapril Unicorn**, should be told to closely monitor for hypoglycaemia, especially during the first month of combined use.

Surgery/Anaesthesia: **Enalapril Unicorn** blocks the formation of angiotensin-II secondary to compensatory renin release in patients undergoing major surgery or during anaesthesia with agents that cause hypotension. If hypotension occurs and is considered to be due to this mechanism, it can be corrected by volume expansion.

Serum potassium: See Section 4.5

Excipients

Enalapril Unicorn contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Enalapril Unicorn contains sodium.

This medicinal product contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially ‘sodium-free’.

4.5 Interaction with other medicines and other forms of interaction

Dual blockade of the RAAS 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 Section 4.3 and 4.4).

Antihypertensive Therapy

The combination of **Enalapril Unicorn** with other antihypertensive medicines may increase the antihypertensive effect, especially in combination with diuretics.

The combination of **Enalapril Unicorn** with ß-adrenergic blocking agents and methyldopa or calcium entry blockers potentiates the hypotensive effects of **Enalapril Unicorn**.

Ganglionic blocking agents or adrenergic blocking agents, combined with **Enalapril Unicorn**, should only be administered with careful observation of the patient.

Because of lack of experience, concomitant treatment of **Enalapril Unicorn** with calcium antagonists is not recommended.

Concomitant use with nitroglycerine and other nitrates, or other vasodilators, may increase the risk of hypotension.

Serum Lithium

Lithium elimination may be reduced. See Section 4.3.

Serum Potassium

Risk factors for the development of hyperkalaemia include renal insufficiency, diabetes mellitus and concomitant use of potassium-sparing diuretics (e.g. spironolactone, triamterene, or amiloride), potassium supplements, or potassium containing salt substitutes. **Enalapril Unicorn** may elevate serum potassium levels in patients with renal impairment. The use of potassium supplements,

potassium sparing diuretics or potassium containing salt substitutes particularly in patients with impaired renal function may lead to a significant increase in serum potassium. See Section 4.3.

Non-steroidal anti-inflammatory medicines including selective cyclooxygenase-2 inhibitors

Non-steroidal anti-inflammatory medicines (NSAIDs) including selective cyclooxygenase-2 inhibitors (COX-2 inhibitors) may reduce the antihypertensive effect of **Enalapril Unicorn**. The co-administration of NSAIDs (including COX-2 inhibitors) with **Enalapril Unicorn** exert an additive effect on the increase in serum potassium, and may result in a deterioration of renal function, including acute renal failure, especially in patients with compromised renal function (such as the elderly or patients who are volume-depleted, including those on diuretic therapy).

Gold

Nitritoid reactions (symptoms include facial flushing, nausea, vomiting and hypotension) have been reported in patients on therapy with injectable gold (sodium aurothiomalate) and concomitant **Enalapril Unicorn** therapy.

Antidiabetics

Concomitant administration of **Enalapril Unicorn** and antidiabetic medicines (insulins, 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.

Others

Concomitant use of general anaesthetic medicinal products, tricyclic antidepressants and antipsychotics with **Enalapril Unicorn** may result in further reduction of blood pressure.

Concomitant administration of allopurinol, cytostatic or immuno-suppressive agents, systemic corticosteroids or procainamide with **Enalapril Unicorn** may increase the risk for leucopenia (see Section 4.4. *Neutropenia/Agranlocytosis*).

Concomitantly administered cyclosporin increases the risk of hyperkalaemia with **Enalapril Unicorn**.

Since sympathomimetics may reduce the antihypertensive effects of **Enalapril Unicorn**, careful monitoring of blood pressure should occur when these medicines are used concomitantly with **Enalapril Unicorn**.

Alcohol enhances the hypotensive effect of concomitantly administered **Enalapril Unicorn**.

Concomitant use of fluoroquinolones and ACE inhibitors/renin-angiotensin receptor blockers may precipitate acute kidney injury. See Section 4.3.

A case series of 16 reports of acute kidney injury (AKI) associated with enalapril and ciprofloxacin as co-suspect or interacting medicines was identified in VigiBase, the WHO global database of individual case safety reports. Analysis of 11 cases indicated that in most patients although clinical conditions and a number of medicines were likely to have increased their risk of AKI, including ACE inhibitor-related AKI, the event did not occur until after a ciprofloxacin prescription, lending weight to ciprofloxacin being the cause or a combined action of ciprofloxacin and enalapril. Furthermore, the interaction between ACE inhibitors and fluoroquinolones to precipitate acute kidney injury is a class effect for all ACE inhibitors and not just enalapril, and also a class effect of all the fluroquinolones not just with ciprofloxacin. Thus, concomitant use of fluoroquinolones and ACE inhibitors/renin-angiotensin receptor blockers may precipitate acute kidney injury. See Section 4.3.

4.6 Fertility, pregnancy and lactation

The use of **Enalapril Unicorn** is contraindicated during pregnancy. Pregnant women should be informed of the potential hazards to the foetus and must not take **Enalapril Unicorn** during pregnancy (see Section 4.3). 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 **Enalapril Unicorn** should be stopped immediately and if appropriate, alternative therapy should be started. Foetal exposure to ACE inhibitors during the first trimester of pregnancy has been reported to be associated with an increased risk of malformations of the cardiovascular (atrial and/or ventricular septal defect, pulmonic stenosis, patent ductus arteriosus) and central nervous system (microcephaly spins bifida) and of kidney malformations. **Enalapril Unicorn** 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 in new-borns, have been reported after administration of **Enalapril Unicorn** during the second and third trimester. Cases of defective skull ossification have been observed. Prematurity and low birth mass can occur (see Section 4.3).

Lactation - Enalapril and enalaprilat are secreted into the breast milk. **Enalapril Unicorn** is contra-indicated in women breast-feeding their babies.

4.7 Effects on ability to drive and use machines

Enalapril Unicorn may cause dizziness or weariness. Patients should be warned not to drive or use machines, until their individual susceptibility to the effects of **Enalapril Unicorn** is known.

4.8 Undesirable effects

System Organ Class	**Frequent**	**Less frequent**
Blood and the lymphatic system disorders		**Anaemia (including aplastic and haemolytic), neutropenia, decreases in haemoglobin, decreases in haematocrit, thrombocytopenia,**

		agranulocytosis, bone marrow depression, pancytopenia, lymphadenopathy, autoimmune diseases.
Immune system disorders		**Anaphylactoid reactions, hypersensitivity/angioneurotic oedema: angioedema of the face, extremeties, lips, tongue, glottis and/or larynx.**
Endocrine disorders		**Syndrome of inappropriate antidiuretic hormone secretion (SIADH).**
Metabolism and nutrition disorders		**Hypoglycemia (see Section 4.4)**
Nervous system disorders	**Headache, depression.**	**Confusion, somnolence, insomnia, nervousness, paraesthesia, vertigo, dream abnormality, sleep disorders.**
Eye disorders	**Blurred vision.**	
Ear and labyrinth disorders		**Tinnitus.**
Cardiac disorders	**Dizziness, hypotension (including orthostatic hypotension), syncope,**	**Raynaud's phenomenon, orthostatic hypotension, palpitations, flushing,**

	chest pain, rhythm disturbances, angina pectoris, tachycardia.	**myocardial infarction or cerebrovascular accident, possibly secondary to excessive hypotension in high risk patients (see Section 4.4).**
Respiratory, thoracic and mediastinal disorders	**Cough, dyspnoea.**	**Rhinorrhoea, sore throat and hoarseness, bronchospasm/asthma, pulmonary infiltrates, rhinitis, allergic alveolitis/eosinophilic pneumonia.**
Gastrointestinal disorders	**Nausea, diarrhoea, abdominal pain, taste alteration.**	**Ileus, pancreatitis, vomiting, dyspepsia, constipation, anorexia, gastric irritations, dry mouth, peptic ulcer, stomatitis/aphthous ulcerations, glossitis, intestinal angioedema.**
Hepatobiliary disorders		**Hepatic failure, hepatitis – ether hepatocellular or cholestatic, hepatitis including necrosis, cholestasis (including jaundice).**

Skin and subcutaneous tissue disorders	**Rash.**	**Diaphoresis, pruritus, urticarial, alopecia, erythema multiforme, Stevens-Johnson syndrome, exfoliative dermatitis, toxic epidermal nerolysis, pemphigus, erythroderma.** **A symptom complex has been reported which may include some or all of the following: fever serositis, vasculitis, myalgia/myositis, arthralgia/arthritis, a positive anti-nuclear antibody (ANA), elevated erythrocyte sedimentation rate (ESR), eosinophilia, and leucocytosis, rash, photosensitivity or other dermatologic manifestations may occur.**
Musculoskeletal and connective tissue disorders		**Muscle cramps.**

Renal and urinary disorders		**Renal dysfunction, renal failure, proteinuria, oliguria.**
Reproductive system and breast disorders		**Impotence, gynaecomastia.**
General disorders and administration site conditions	**Asthenia, fatigue.**	**Flushing, malaise, fever.**
Investigations	**Hyperkalaemia, increases in serum creatinine.**	**Increases in blood urea, hyponatraemia, elevations of liver enzymes, elevations of serum bilirubin.**

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. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the **"6.04 Adverse Drug Reactions Reporting Form"**, found online under SAHPRA's publications: https://www.sahpra.org.za/

4.9 Overdose

Limited data are available for overdosage in humans. The most prominent feature of overdosage is hypotension, six hours after ingestion of the tablets, as well as stupor.

Symptoms associated with overdosage of **Enalapril Unicorn** may include circulatory shock, electrolyte disturbances, renal failure, hyperventilation, tachycardia, palpitations, bradycardia, dizziness, anxiety, and cough.

The recommended treatment of overdosage with **Enalapril Unicorn** is symptomatic and supportive. An intravenous infusion of 0,9 % sodium chloride may be considered. If available, treatment with angiotensin II infusion and/or intravenous sympathomimetics may also be considered.

Enalapril Unicorn may be removed from the general circulation by haemodialysis. Vital signs, serum electrolytes and creatinine concentrations should be monitored.

5 PHARMACOLOGICAL PROPERTIES

5.4 Pharmacodynamic properties

Category and class: A 7.1.3 Vascular medicines - Other hypotensives

Pharmacotherapeutic group: Angiotensin Converting Enzyme (ACE) inhibitor- ATC Code: C09AA02

Following oral administration and absorption, enalapril is hydrolysed to enalaprilat which is a non-sulfhydryl angiotensin converting enzyme (ACE) inhibitor. Enalapril is a derivative of two amino acids; L-alanine and L-proline. ACE is a peptidyl dipeptidse which catalyses the conversion of angiotensin I to the pressor substance angiotensin II. This results in reduced plasma renin activity and decreased aldosterone secretion. The blood pressure lowering effect of enalapril is primarily through suppression of the renin- angiotensin- aldosterone system.

5.5 Pharmacokinetic properties

Absorption:

Oral enalapril is absorbed, with peak serum concentrations of enalapril occurring within one hour. Based on urinary recovery, the extent of absorption of enalapril from oral enalapril tablet is approximately 60 %. The absorption of oral enalapril is not influenced by the presence of food in the gastrointestinal tract.

Following absorption, oral enalapril is rapidly and extensively hydrolysed to enalaprilat, an angiotensin converting enzyme inhibitor. Peak serum concentrations of enalaprilat occur about 4

hours after an oral dose of enalapril tablet. The effective half-life of enalaprilat following multiple doses of oral enalapril is 11 hours. In subjects with normal renal function, steady-state serum concentrations of enalaprilat were reached after 4 days of treatment.

Distribution:

Over the range of concentrations which are therapeutically relevant, enalaprilat binding to human plasma proteins does not exceed 60 %.

Biotransformation:

Except for conversion to enalaprilat, there is no evidence for significant metabolism of enalapril.

Excretion:

Excretion of enalaprilat is primarily renal. The principal components in urine are enalaprilat, accounting for about 40 % of the dose, and intact enalapril (about 20 %).

Renal impairment:

The exposure of enalapril and enalaprilat is increased in patients with renal insufficiency. In patients with mild to moderate renal insufficiency (creatinine clearance 40-60 ml/min) steady state AUC was approximately two-fold higher than in patients with normal renal function after administration of 5 mg once daily. In severe renal impairment (creatinine clearance ≤ 30 ml/min), AUC was increased approximately 8-fold. The effective half-life of enalaprilat following multiple doses of enalapril maleate is prolonged at this level of renal insufficiency and time to steady state is delayed (see Section 4.2) Enalaprilat may be removed from the general circulation by haemodialysis.

6 PHARMACEUTICAL PARTICULARS

6.4 List of excipients

ENALAPRIL UNICORN 5

- Colloidal anhydrous silica,
- Croscarmellose sodium (AC-DI-SOL),
- Lactose (Pharmatose DCL 11),
- Maleic acid,
- Microcrystalline cellulose (PH112),
- Zinc stearate.

ENALAPRIL UNICORN 10

- Colloidal anhydrous silica,
- Croscarmellose sodium (AC-DI-SOL),
- Ferric oxide red (Cl No. 77491),
- Lactose (Pharmatose DCL 11),
- Maleic acid,
- Microcrystalline cellulose (PH112),
- Zinc stearate.

ENALAPRIL UNICORN 20

- Colloidal anhydrous silica,
- Croscarmellose sodium (AC-DI-SOL),
- Ferric oxide red (Cl No. 77491),
- Ferric oxide yellow (Cl No. 77492),
- Lactose (Pharmatose DCL 11),
- Maleic acid,
- Microcrystalline cellulose (PH112),
- Zinc stearate.

6.5 Incompatibilities

Not applicable

6.6 Shelf life

36 months

6.7 Special precautions for storage

Store at or below 25 °C, protected from moisture.

6.8 Nature and contents of container

Enalapril Unicorn 5: Carton containing 4 blister strips of 7 tablets in each blister

Enalapril Unicorn 10: Carton containing 4 blister strips of 7 tablets in each blister

Enalapril Unicorn 20: Carton containing 4 blister strips of 7 tablets in each blister

6.9 Special precautions for disposal

No special requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

Ranbaxy Pharmaceuticals (Pty) Ltd.

14 Lautre Road,

Stormill, Ext. 1

Roodepoort,1724,

South Africa

8 REGISTRATION NUMBER(S)

Enalapril Unicorn 5: 34/7.1.3/0010

Enalapril Unicorn 10: 34/7.1.3/0011

Enalapril Unicorn 20: 34/7.1.3/0012

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

28 September 2000

10 DATE OF REVISION OF THE TEXT

21 November 2022