PROPOSED PROFESSIONAL INFORMATION FOR HUMAN MEDICINES

SCHEDULING STATUS

S3

1 NAME OF THE MEDICINE

BISOPROLOL UNICORN 5

BISOPROLOL UNICORN 10

Strength: 5 mg, 10 mg bisoprolol fumarate

Pharmaceutical form: tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

BISOPROLOL UNICORN 5: Each tablet contains 5 mg bisoprolol fumarate

BISOPROLOL UNICORN 10: Each tablet contains 10 mg bisoprolol fumarate

BISOPROLOL UNICORN 5: contains sugar (135,20 mg) lactose monohydrate)

BISOPROLOL UNICORN 10: contains sugar (130,20 mg) lactose monohydrate)

(see section 4.4).

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

BISOPROLOL UNICORN 5: Mottled pale yellow, round normal convex tablet debossed with 'Bl' break line '5' on one side and plain on the reverse.

BISOPROLOL UNICORN 10: Mottled beige, round normal convex tablet debossed with 'Bl' break line '10' on one side and plain on the reverse.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

BISOPROLOL UNICORN is indicated for the management of mild to moderate essential hypertension and angina pectoris. It may be used alone or in combination with other antihypertensive medicines.

4.2 Posology and method of administration

Posology

Adults:

In all cases the dosage should be adjusted individually, in particular according to the pulse rate and therapeutic success.

Hypertension

The recommended dosage is 5 mg **BISOPROLOL UNICORN** once daily.

If necessary, the dosage may be increased to 10 mg once daily. Individual patients may benefit from a dose of 20 mg once daily.

The maximum recommended dosage is 20 mg once daily.

Angina pectoris

The recommended dosage is 5 mg **BISOPROLOL UNICORN** once daily.

If necessary, the dosage may be increased to 10 mg once daily.

No benefit was shown by increasing the dose to 20 mg once daily.

The maximum recommended dosage is 20 mg once daily.

Special populations

Dosage in hepatic and/or renal insufficiency:

In patients with liver or kidney function disorders of mild to moderate severity: no dosage

adjustment is normally required.

In patients with severe kidney function disorders (creatinine clearance < 30 ml/min) and in patients with severely impaired liver function: do not exceed the daily dose of 10 mg.

There is only limited experience with the use of **BISOPROLOL UNICORN** in dialysis patients. There are no indications of the necessity to alter the dose regimen.

Elderly:

No dose adjustment is normally required.

Paediatric population

There is no therapeutic experience with **BISOPROLOL UNICORN** in children. Its use in children is therefore not recommended (see section 4.4).

Method of administration

5 to 10 mg should be taken once a day in the morning with or without food.

BISOPROLOL UNICORN should be swallowed whole with some liquid in the morning before, during or after breakfast.

The duration of treatment is not limited. It depends upon the nature and severity of the disease.

BISOPROLOL UNICORN therapy should not be stopped abruptly, particularly not in patients with ischaemic heart disease, as this may lead to acute deterioration of the patient's state of health (see section 4.4). If discontinuation of therapy becomes necessary, the dose should be gradually reduced (e.g. halving of the dose at weekly intervals).

4.3 Contraindications

- Hypersensitivity to bisoprolol or to any of the ingredients of **BISOPROLOL UNICORN** (see section 6.1)**.**

- Severe bronchial asthma or chronic obstructive pulmonary disease. Severe forms of peripheral arterial occlusive disease and Raynaud's syndrome.
- Second and third-degree heart (sinoarterial) block and sinus bradycardia (less than 50 beats per minute).
- Uncontrolled cardiac failure.
- Acute heart failure or during episodes of heart failure decompensation requiring I.V. inotropic therapy.
- Cardiogenic shock.
- Second or third degree AV block (without a pacemaker).
- Metabolic acidosis.
- Hypotension (systolic blood pressure < 100 mmHg)
- Sick sinus syndrome.
- Phaeochromocytoma before full alpha blockade is achieved (see section 4.4).
- Hyperthyroidism, as clinical manifestations may be masked.
- Safety and efficacy in children have not been established.
- Pregnancy (see section 4.6).

4.4 Special warnings and precautions for use

In patients undergoing general anaesthesia beta-blockade reduces the incidence of arrhythmias and myocardial ischaemia during induction and intubation, and the post-operative period.

The anaesthetist must be aware of beta-blockade because of the potential for interactions with other medicines, resulting in bradydysrhythmias, attenuation of the reflex tachycardia and the decreased reflex ability to compensate for blood loss

If the decision is made to withdraw **BISOPROLOL UNICORN** before anaesthesia, this should

be done gradually and at least 48 hours should be allowed to elapse between the last dose and surgery.

If **BISOPROLOL UNICORN** is to be continued, care should be taken when using anaesthetics.

Atropine (1-2 mg I.V.) may be used to correct vagal dominance.

The patient must be maintained on their usual dosage peri-operatively to avoid aggravation of angina pectoris or hypertension.

The normal dose should be reduced in elderly patients, or in patients suffering from renal dysfunction (see section 4.2). In the peri-operative period it is generally unwise to reduce the dosage to which the patient is accustomed, as there may be danger of aggravation of angina pectoris or hypertension. A patient's normal tachycardia response to hypovolaemia or blood loss may be obscured during or after surgery. Particular caution should be taken in this regard.

Care should be taken in prescribing **BISOPROLOL UNICORN** together with Class 1 anti-dysrhythmic medicines such as disopyramide, myocardial depressants and inhibitors of AV conduction such as calcium antagonists.

Particular caution should be taken in this regard and in diabetes mellitus, as symptoms and signs of hypoglycaemia may be masked, and as responses to hypoglycaemia are diminished.

Caution should be exercised when transferring a patient from clonidine. The withdrawal of clonidine may result in the release of large amounts of catecholamines that may give rise to a hypertensive crisis. If **BISOPROLOL UNICORN** is administered in these circumstances, the unopposed alpha receptor stimulation may potentiate this effect.

If **BISOPROLOL UNICORN** and clonidine are given concurrently, the clonidine should not be discontinued until several days after the withdrawal of **BISOPROLOL UNICORN**, as severe rebound hypertension may occur.

BISOPROLOL UNICORN should be used with caution in combination with verapamil in patients with impaired ventricular function. This combination should not be given to patients with conduction abnormalities. Neither medicine should be administered intravenously within 48 hours of discontinuing the other. The intravenous administration of calcium antagonists and antidysrhythmic medicines is not recommended during therapy with **BISOPROLOL UNICORN**.

BISOPROLOL UNICORN modifies the tachycardia associated with hypoglycaemia. Patients with phaeochromocytoma usually require treatment with an alpha-adrenergic blocker (see section 4.3). In patients with phaeochromocytoma **BISOPROLOL UNICORN** must not be administered until after full alpha-receptor blockade has been established. Beta blockade is seldom required in the pre-operative preparation of these patients.

Patients with psoriasis or with a history of psoriasis may have their conditions worsened by **BISOPROLOL UNICORN**, and therefore must only be given **BISOPROLOL UNICORN** after careful consideration of the risks and benefits.

The symptoms of hyperthyroidism may be masked under treatment with **BISOPROLOL UNICORN** (see section 4.3).

The symptoms of thyrotoxicosis may be masked under treatment with **BISOPROLOL UNICORN.**

The sensitivity towards allergens and anaphylactic reactions may be increased by **BISOPROLOL UNICORN**. Treatment with epinephrine (adrenaline) does not always produce the required therapeutic effect.

Intensification of peripheral arterial occlusive disease may happen, especially during the start of treatment with **BISOPROLOL UNICORN**. **BISOPROLOL UNICORN** may aggravate the symptoms of peripheral arterial occlusive disease (PAOD) or Raynaud's syndrome (due to unopposed arteriolar alpha-sympathetic activation). Severe peripheral vascular disease and even peripheral gangrene may be precipitated.

BISOPROLOL UNICORN must be used with caution in fasting patients.

Beta-blockers, including **BISOPROLOL UNICORN**, may increase the number of chest pain attacks in patients who have Prinzmetal’s angina.

Cases of coronary vasospasm have been observed. Despite its high $beta_1$-selectivity, angina attacks cannot be completely excluded when **BISOPROLOL UNICORN**, is administered to patients with Prinzmetal's angina. Utmost caution must be exercised.

BISOPROLOL UNICORN may be used only with special caution in patients with First degree AV block.

Treatment with **BISOPROLOL UNICORN** must not be withdrawn abruptly unless clearly indicated (see section 4.2).

Abrupt discontinuation of therapy with **BISOPROLOL UNICORN** may cause exacerbation of angina pectoris in patients suffering from ischaemic heart disease, myocardial infarction, ventricular dysrhythmias and in some cases could lead to sudden death.

Discontinuation of **BISOPROLOL UNICORN** should be gradual over a period of 1 to 2 weeks, and patients should be advised to limit the extent of their physical activity during the period that **BISOPROLOL UNICORN** is being discontinued.

Caution is warranted when treating patients with hypertension or angina pectoris and

concomitant heart failure with **BISOPROLOL UNICORN**.

Digitalisation of patients receiving long-term beta-blocker therapy including **BISOPROLOL UNICORN** may be necessary if congestive cardiac failure is likely to develop. This combination can be considered despite the potentiation of the negative chronotropic effect of the two medicines. Careful control of dosages, and of the individual patient's response (and notably pulse rate), is essential in this situation.

Beta-blockers, including **BISOPROLOL UNICORN**, may unmask myasthenia gravis.

Although cardioselective ($beta_1$) beta-blockers may have less effect on lung function than nonselective beta-blockers, these should be avoided in patients with obstructive airways diseases, unless there are compelling clinical reasons for their use. Where such reasons exist, **BISOPROLOL UNICORN** may be used with caution. In bronchial asthma or other chronic obstructive pulmonary diseases, which may cause symptoms, concomitant bronchodilating therapy is recommended. Occasionally an increase of the airway resistance may occur in patients with asthma, therefore, the dose of $beta_2$-stimulants may have to be increased.

Paediatric population

Safety and efficacy of **BISOPROLOL UNICORN** have not been established in children.

BISOPROLOL UNICORN contains sugar (lactose). Patients with rare hereditary conditions or a history of galactose intolerance e.g. galactosaemia, Lapp lactase deficiency or glucose-galactose malabsorption should not take **BISOPROLOL UNICORN.**

Contains lactose which may have an effect on the glycaemic control of patients with diabetes mellitus.

4.5 Interaction with other medicines and other forms of interaction

Combinations not recommended

• Calcium antagonists such as verapamil, and to a lesser degree diltiazem, negatively influence contractility and atrio-ventricular conduction (see section 4.4). In patients on **BISOPROLOL UNICORN**, the I.V. administration of verapamil may cause profound atrio-ventricular block and hypotension. The use of **BISOPROLOL UNICORN** in combination with calcium antagonists is therefore not recommended.

• Clonidine and other centrally acting antihypertensive medicines such as methyldopa, moxonodine and rilmenidine may further decrease heart rate, cardiac output and vasodilation if taken together with **BISOPROLOL UNICORN**.

Beta-blockers, such as **BISOPROLOL UNICORN** may exacerbate the “rebound hypertension” which can occur in case of abrupt withdrawal of centrally acting antihypertensive medicines (e.g. Clonidine). If the two medicines are co-administered, the β-blocker should be withdrawn several days before discontinuing clonidine. If replacing clonidine by β-blocker therapy, the introduction of β-blockers should be delayed for several days after clonidine administration has stopped.

Combinations to be used with caution

• Concomitant use of **BISOPROLOL UNICORN** with hypoglycaemic medicines, phenothiazines and various anti-dysrhythmic medicines can have life-threatening consequences, e.g.

- profound hypoglycaemia with oral hypoglycaemic medicines and insulin. Blockade of beta-adrenoceptors may mask symptoms of hypoglycaemia (see section 4.4);
- myocardial depression with anti-dysrhythmic medicines.

• Beta-adrenoceptor stimulating medicines (e.g. isoprenaline, dobutamine) may antagonise the effects of **BISOPROLOL UNICORN**. Combination with **BISOPROLOL UNICORN** may reduce the effect of both medicines. Higher doses of epinephrine (adrenaline) may be necessary for treatment of allergic reactions.

• Sympathomimetics that activate both beta- and alpha-adrenoceptors (e.g. norepinephrine(noradrenaline), epinephrine (adrenaline)): Combination with **BISOPROLOL UNICORN** may unmask the alpha-adrenoceptor-mediated vasoconstrictor effect of these medicines leading to blood pressure increase and exacerbated intermittent claudication.

• Alpha-adrenoceptor stimulants as well as adrenergic neurone blocking medicines may lead to life-threatening vasoconstriction in combination with **BISOPROLOL UNICORN**.

• **BISOPROLOL UNICORN** and digoxin may be used concomitantly for patients with congestive heart failure provided that the pulse rate and patient response is monitored.

• Dihydropyridine-type calcium antagonists such as nifedipine and amlodipine, should not be used in combination with **BISOPROLOL UNICORN** since this may increase the risk of hypotension. In patients with heart failure, an increase in the risk of further deterioration of the ventricular pump function cannot be excluded.

• Atrio-ventricular conduction time, as well as negative inotropic effect, may be increased when **BISOPROLOL UNICORN** is used concurrently with Class-I antidysrhythmic medicines (e.g. disopyramide and quinidine, lidocaine, phenytoin, flecainide, propafenone). Atrio-ventricular conduction time may also be increased when **BISOPROLOL UNICORN** is taken concomitantly with Class-III antidysrhythmic medicines (e.g. amiodarone).

• Parasympathometic medicines may increase atrio-ventricular conduction time and the risk of bradycardia if used concomitantly with **BISOPROLOL UNICORN.**

• Anaesthesia: Attenuation of the reflex tachycardia and increase of the risk of hypotension.

• Alcohol may potentiate the hypotensive effects of beta-blockers.

• The systemic effects of **BISOPROLOL UNICORN** may be potentiated by topical beta-blockers (e.g. eye drops for glaucoma treatment).

• Digoxin (Digitalis glycosides) may reduce heart rate and increase atrio-ventricular conduction time when used in combination with **BISOPROLOL UNICORN.**

• When taken with **BISOPROLOL UNICORN**, non-steroidal anti-inflammatory drugs (NSAID's) may reduce the hypotensive effects of **BISOPROLOL UNICORN**.

• Concomitant use of **BISOPROLOL UNICORN** with anti- antihypertensive medicines and other blood pressure lowering medicines (e.g barbiturates, phenothiazides and tricyclic anti-depressants) may increase the risk of hypotension.

• Moxisylyte, when taken together with **BISOPROLOL UNICORN**, may cause severe postural hypotension.

Combinations to be considered

• Antimalarials such as halofantrine, mefloquine and quinine, when taken concomitantly with **BISOPROLOL UNICORN**, may increase the risk of bradycardia and other cardiac conduction defects.

• The hypotensive effects of **BISOPROLOL UNICORN** may be enhanced by concomitant use with monoamino oxidase inhibitors (except MAO-B inhibitors), but also with a risk for hypertensive crisis.

• Rifampicin may reduce plasma concentrations of bisoprolol as contained in **BISOPROLOL**

UNICORN. Slight reduction of the half-life of bisoprolol possible due to the induction of hepatic metabolising enzymes. Normally no dosage adjustment is necessary.

• Ergotamine derivatives: Exacerbation of peripheral circulatory disturbances. In high-dose salicylate administration the toxic effect of salicylates on the central nervous system may be enhanced.

4.6 Fertility, pregnancy and lactation

Pregnancy

The use of **BISOPROLOL UNICORN** during pregnancy is not recommended (see section 4.3).

BISOPROLOL UNICORN has pharmacological effects that may cause harmful effects on pregnancy and/or the foetus/newborn. **BISOPROLOL UNICORN** reduce placental perfusion, which has been associated with growth retardation, intrauterine death, abortion or early labour.

Administration of **BISOPROLOL UNICORN** to pregnant mothers shortly before birth or during labour may result in hypotonia, bradycardia, cardiovascular collapse, cardiac and pulmonary complications or hypoglycaemia in the foetus and newborn.

Breastfeeding

It is not known whether **BISOPROLOL UNICORN** is excreted in human milk.
Mothers on **BISOPROLOL UNICORN** should not breastfeed their infants.

Fertility

No effect on fertility was observed in male or female rats treated with bisoprolol at oral doses up to 150 mg/kg/day.

4.7 Effects on ability to drive and use machines

"Bisoprolol, as in **BISOPROLOL UNICORN**, may cause dizziness, tiredness or muscle aches therefore, it may adversely affect affect the patient's ability to drive or use machinery

4.8 Undesirable effects

System Organ Class	Frequency	Side effects
Blood and lymphatic system disorders	*Less frequent*	Agranulocytosis, leukopenia, thrombocytopenia.
	Frequency unknown	Non-thrombocytopenic purpura, transient eosinophilia
Immune system disorders	*Less frequent*	Hypersensitivity (allergic) reactions (itching, flush, rash and angioedema).
	Frequency unknown	Systemic Lupus Erythematosus (SLE)
Metabolism and nutrition disorders	*Frequency unknown*	Metabolic disturbances, hypoglycaemia, increase in uric acid levels, hypercholesterolaemia, hyperglycaemia, Increased triglycerides, increased liver enzymes (ALAT, ASAT).
Psychiatric disorders	*Less frequent*	Amnesia, *a*nxiety, nervousness, mental depression, sleep disorders or trouble sleeping, nightmares and vivid dreams, hallucinations, confusion.
	Frequency unknown	Restlessness, psychosis.
Nervous system disorders	*Frequent*	Dizziness*, drowsiness, mild headache*, unusual tiredness or weakness
	Less frequent	Syncope.

System Organ Class	**Frequency**	**Side effects**
	Frequency unknown	Paraesthesia
Gastrointestinal disorders	*Frequent*	Nausea, vomiting, diarrhoea, constipation
	Frequency unknown	Mass gain, stomatitis, abdominal cramps, dry mouth.
Hepato-biliary disorders	*Less frequent*	Hepatotoxicity, hepatitis.
Musculoskeletal and connective tissuedisorders	*Less frequent*	Back pain or joint pain, chest pain, muscle cramps, skeletal muscle weakness, muscle ache.
	Frequency unknown	Myopathy.
Eye disorders	*Less frequent*	Conjunctivitis, Dry, sore eyes, reduced tear flow (to be considered if the patients uses contact lenses)
	Frequency unknown	Disturbances of vision
Ear and labyrinth disorders	*Less frequent*	Hearing disorders
	Frequency unknown	Transient hearing loss
Cardiac disorders	*Less frequent*	AV-conduction disturbances, bradycardia and congestive cardiac failure, dysrhythmias, worsening pre-existing heart failure.
	Frequency unknown	Heart block.
Vascular disorders	*Frequent*	Exacerbation of peripheral vascular diseases, hypotension, feeling of coldness or numbness in the extremities,
	Less frequent	Orthostatic hypotension, paradoxical hypertension, the development of Raynaud’s phenomenon, peripheral gangrene may be precipitated, reduced

System Organ Class	Frequency	Side effects
		peripheral circulation, cyanosis of extremities.
	Frequency unknown	Fluid retention
Skin and subcutaneous tissue disorders	*Less frequent*	Skin rash, psoriasiform eruption (Beta-blockers can trigger psoriasis, aggravate the condition or lead to psoriasis form rash), reversible alopecia, itching
	Frequency unknown	Perspiration, pruritus
Respiratory, thoracic and mediastinal disorders	*Less frequent*	Bronchoconstriction bronchospasm (in patients with bronchial asthma or a history of obstructive airways disease), shortness of breath or dyspnoea, bronchitis and other chronic pulmonary diseases. Allergic rhinitis, nasal congestion.
	Frequency unknown	Pneumonitis, pulmonary fibrosis, pleurisy.
Reproductive system and breast disorders	*Frequent*	Decreased sexual ability
	Less frequent	Impotence, potency disorders
General disorders and administrative site conditions	*Frequent*	Fatigue*, lassitude
	Less frequent	Asthenia, oedema
	Frequency unknown	Sclerosing peritonitis, retroperitoneal fibrosis.
Investigations	*Less frequent*	Raised liver enzymes (ALAT, ASAT), increased triglycerides, increase in anti-nuclear antibodies.

**This symptom especially occurs at the beginning of therapy. It is generally mild and often disappears within 1 – 2 weeks.*

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/Publications/Index/8. Reporting can also be done directly to Unicorn Pharmaceuticals at: **vigilance@unicornpharma.co.za .**

4.9 Overdose

Symptoms

(See section 4.8)

Overdosage may produce bradycardia and severe hypotension.

Bronchospasm and bronchoconstriction may be produced in certain individuals as well as acute cardiac insufficiency, cardiac conduction block, heart failure, cardiogenic shock and hypoglycaemia.

Coma and convulsions have also been reported, and some patients may develop severe and occasionally fatal cardiovascular depression.

Cases of overdose should be observed for at least 4 hours, as apnoea and cardiovascular collapse may appear suddenly.

Treatment

Generally, in cases of overdose, the patient should stop taking **BISOPROLOL UNICORN** and supportive and symptomatic treatment should be provided.

Repeated activated charcoal is necessary in severe overdose

The data available suggest that bisoprolol is not dialysable to any extent.

Atropine may be administered intravenously to treat severe bradycardia. If the response is

inadequate, isoprenaline or another medicine with positive chronotropic properties may be given cautiously. Under some circumstances, transvenous pacemaker insertion may be necessary

Alternatively, dobutamine may be required to reverse beta-blockade. Cardiac pacing may be required for severe bradycardia.

Hypotension: Vasopressors and I.V. fluids should be administered.

Glucagon may be given intravenously, with sympathomimetics used as an alternative or given with glucagon.

AV block (second or third degree): Monitor patients closely and treat with isoprenaline infusion or insert a cardiac pacemaker.

Acute worsening of heart failure: Recommended treatment includes I.V. diuretics, inotropic medicines and vasodilating medicines.

Bronchospasm should be treated with bronchodilator therapy such as isoprenaline, β2-sympathomimetic medicines and/or aminophylline. Beta-agonist (e.g. salbutamol) or xanthines may also be given.

Hypoglycaemia: I.V. glucose or glucagon can be administered.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 5.2 Adrenolytics (sympathicolytic).

ATC Code: C07A B07

Bisoprolol is a selective β1-adrenoceptor antagonist with low β2 receptor affinity. It blocks beta-adrenergic receptors in the heart and the juxtaglomerular apparatus (kidneys), thus decreasing the excitability of the heart, the cardiac output, the oxygen myocardial consumption and the release of renin from the kidneys. Another factor that may be involved in contributing to the antihypertensive action is the decrease of the tonic sympathetic outflow

from the vasomotor centres in the brain. It is devoid of intrinsic sympathomimetic and membrane-stabilising activity. It reduces blood pressure, and by blockade of the cardiac ß1-receptors, reduces heart rate and depresses plasma renin levels.

5.2 Pharmacokinetic properties

Absorption:

Because of its moderate hepatic metabolism, it is subject only to a very small hepatic first pass metabolism. Bisoprolol is well absorbed following oral administration with a resultant bioavailability of about 90 %. Absorption is not affected by food. T_{max} varies from 1 to 4 hours.

Distribution:

Bisoprolol is about 30 % bound to plasma proteins. The distribution volume is 3,5 l/kg. Total clearance is approximately 15 l/h.

Biotransformation:

Bisoprolol undergoes minimal hepatic first-pass metabolism. About 50 % of a dose is metabolised in the liver and the remainder is excreted unchanged via the kidneys. None of the metabolites have ß1-receptor blocking action.

Elimination:

Bisoprolol excreted predominantly via the urine as unaltered substance and metabolites. The plasma elimination half-life is approximately 10 to 12 hours and the duration of action is about 24 hours. There are no active metabolites in man. Less than 2 % of the dose is excreted in the faeces.

5.3 Preclinical safety data

Not Applicable

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Crospovidone, lactose monohydrate, magnesium stearate, microcrystalline cellulose. The following colourants are also included iron oxide yellow (**BISOPRLOL UNICORN 5** only), iron oxide beige (**BISOPROLOL UNICORN 10** only).

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at or below 25 °C. Protect from light.

Keep the blisters in the carton until required for use.

6.5 Nature and contents of container

Opaque or clear Al/PVC/PVdC blister packs containing 30 tablets.

6.6 Special precautions for disposal and other handling

No special requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

Unicorn Pharmaceuticals (Pty) Ltd

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Woodstock

Cape Town

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8 REGISTRATION NUMBER(S)

BISOPROLOL UNICORN 5: 38/5.2/0050

BISOPROLOL UNICORN 10: 38/5.2/0052

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23 July 2010

10 DATE OF REVISION OF THE TEXT

06 December 2023