SCHEDULING STATUS

S3

1 NAME OF THE MEDICINE

BIO-ATENOLOL 50 (Tablets)

BIO-ATENOLOL 100 (Tablets)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

BIO-ATENOLOL 50 contains 50 mg atenolol.

BIO-ATENOLOL 100 contains 100 mg atenolol.

Contains sugar (BIO-ATENOLOL 50 contains 90 mg and BIO-ATENOLOL 100 contains 180 mg lactose monohydrate).

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablets

BIO-ATENOLOL 50: Orange coloured biconvex film-coated tablet, having a score-line on one side and plain on the other side.

BIO-ATENOLOL 100: Orange coloured biconvex film-coated tablet, having score-line on one side and plain on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Hypertension.

Management of angina pectoris.

Myocardial infarction: BIO-ATENOLOL reduces cardiovascular mortality in patients who survived the acute phase of myocardial infarction and are clinically stable.

4.2 Posology and method of administration

Posology

In the treatment of hypertension, BIO-ATENOLOL is usually given orally in a dose of 100 mg daily as a single dose or in divided doses. It is unlikely that additional benefit will be obtained with higher doses of BIO-ATENOLOL.

The treatment of angina pectoris, a single dose of 100 mg daily or 50 mg twice daily has been recommended. It is unlikely that additional benefit will be obtained with higher doses.

Special Populations

Elderly and renal dysfunction:

The normal dose should be reduced in elderly patients and may need to be reduced in patients suffering from renal dysfunction.

Renal failure:

Since BIO-ATENOLOL is excreted via the kidneys, dosage should be adjusted in cases of severe impairment of renal function. No significant accumulation of BIO-ATENOLOL occurs at a glomerular filtration rate (GFR) greater than 35 mL/min/1,73 m^2 (normal range is 100-150 mL/min/1,73 m^2). For patients with a creatinine clearance of 15-35 mL/min/1,73m^2 (equivalent to serum creatinine of 300-600 micromol/litre) the oral dose should be 50 mg daily or 100 mg once every two days.

For patients with a creatinine clearance of < 15 mL/min/1,73 m^2 (equivalent to serum creatinine of > 600 micromol/litre) the oral dose should be 25 mg daily or 50 mg on alternate days or 100 mg once every four

days. Patients on haemodialysis should be given 50 mg orally after each dialysis; this should be done under hospital supervision as marked falls in blood pressure can occur.

Paediatric population

There is no experience in children with BIO-ATENOLOL and for this reason it is not recommended for use in children.

Method of administration

For oral administration.

4.3 Contraindications

BIO-ATENOLOL should not be used in patients:

- who are hypersensitive to atenolol or to any of the excipients of BIO ATENOLOL listed in section 6.1.
- with cardiogenic shock
- with second- or third-degree heart block
- with bradycardia
- with severe peripheral arterial circulatory disturbances.
- with uncontrolled heart failure
- with untreated phaeochromocytoma
- with sick sinus syndrome
- with hypotension
- with metabolic acidosis (e.g., in diabetes)
- after prolonged fasting.

4.4 Special warnings and precautions for use

Patients with phaeochromocytoma usually require treatment with an alpha-adrenergic blocker (see section

4.3).

Particular caution should be exercised with patients suffering from the following: asthma, bronchitis and chronic respiratory diseases. Bronchoconstriction may occur in patients suffering from asthma, bronchitis and other chronic pulmonary diseases.
Congestive cardiac failure and marked bradycardia may also manifest (see section 4.3). A variety of neuropsychiatric disorders, ranging from vague fatigue and nightmares to overt psychosis, have been observed.

Although cardio selective ($beta_1$) beta-blockers may have less effect on lung function than non-selective beta-blockers, these should be avoided in patients with reversible obstructive airway disease, unless there are compelling clinical reasons for their use. Where such reasons exist BIO-ATENOLOL may be used with caution (see section 4.3).

Occasionally, some increase in airways resistance may occur in asthmatic patients however, this may usually be reversed by commonly used dosage of bronchodilators such as salbutamol or isoprenaline.

The following may occur: exacerbation of peripheral vascular disease, or the development of Raynaud's phenomenon (due to unopposed arteriolar alpha-sympathetic activation) (see section 4.3), sexual impotence, hypoglycaemia, skeletal muscle weakness and gastro-intestinal disturbances. Severe peripheral vascular disease and even peripheral gangrene may be precipitated. Adverse reactions are more common in patients with renal decompensation, and in patients who receive the medicine intravenously.

It is dangerous to administer beta-adrenoceptor blocking medicines, such as BIO-ATENOLOL, concomitantly with the following medicines: phenothiazines, hypoglycaemic medicines and various anti-dysrhythmic medicines. Such medicine interactions can have life threatening consequences (see section 4.5).

Although contraindicated in uncontrolled heart failure (see section 4.3), BIO-ATENOLOL may be used in patients whose signs of heart failure have been controlled. Caution must be exercised in patients whose cardiac reserve is poor.

SPECIAL NOTE: digitalisation of patients receiving long-term beta-blocker therapy 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.
It should only be given to patients with congestive cardiac failure when fully digitalised and only then with extreme caution.

Abrupt discontinuation of therapy may cause exacerbation of angina pectoris in patients suffering from ischaemic heart disease. Discontinuation of therapy should be gradual, and patients should be advised to limit the extent of their physical activity during the period that the medicine is being discontinued. Patients should be followed during withdrawal, especially those with ischaemic heart disease.

BIO-ATENOLOL may increase the number and duration of angina attacks in patients with Prinzmetal's angina due to unopposed alpha-receptor mediated coronary artery vasoconstriction. BIO-ATENOLOL is a $beta_1$ selective betablocker; consequently, its use may be considered although utmost caution must be exercised.

Due to its negative effect on conduction time, caution must be exercised if it is given to patients with first-degree heart block.

BIO-ATENOLOL may mask the symptoms of hyperthyroidism. The effects of other myocardial depressant

medicines such as quinidine, procainamide or lignocaine and medicines which interfere with calcium transport such as verapamil may be enhanced by BIO-ATENOLOL (see section 4.5). Myocardial depressants such as chloroform or ether must be avoided.

May mask the symptoms of hypoglycaemia, in particular, tachycardia.

BIO-ATENOLOL may mask the signs of thyrotoxicosis.

The effects of BIO-ATENOLOL may be enhanced by adrenergic neurone blocking medicines such as guanethidine and bethanidine, catecholamine depleting medicines such as reserpine and the hypotensive effects by diuretics.

BIO-ATENOLOL may enhance some of the cardiac effects of digitalis and diminish others (see section 4.5).

BIO ATENOLOL will reduce heart rate as a result of its pharmacological action. In the rare instances when a treated patient develops symptoms which may be attributable to a slow heart rate and the pulse rate drops to less than 50-55 bpm at rest, the dose should be reduced.

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 BIO-ATENOLOL is administered in these circumstances, the unopposed alpha receptor stimulation may potentiate this effect (see section 4.5). If a BIO-ATENOLOL and clonidine are given concurrently, the clonidine should not be discontinued until several days after the withdrawal of BIO-ATENOLOL, as severe rebound hypertension may occur (see section 4.5).

Anaesthesia: Awareness by the anaesthetist that BIO-ATENOLOL are being taken is of greatest importance **(**see section 4.3). Great care should be exercised in giving BIO-ATENOLOL to patients undergoing anaesthesia.

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 tachycardic response to hypovolaemia or blood loss may be obscured during or after surgery. Particular caution should be taken in this regard.

When a patient is scheduled for surgery, and a decision is made to discontinue BIO-ATENOLOL therapy, this should be done at least 24 hours prior to the procedure. The risk-benefit assessment of stopping beta-blockade should be made for each patient. If treatment is continued, and anaesthetic with little negative inotropic activity should be selected to minimise the risk of myocardial depression. The patient may be protected against vagal reactions by intravenous administration of atropine.

The effects of BIO-ATENOLOL are diminished by beta-adrenoceptor stimulating medicines such as isoprenaline; the hypotensive effect of BIO-ATENOLOL may be dangerously reversed, and the peripheral vasoconstrictor effects enhanced by alpha-adrenoceptor stimulating medicines such as noradrenaline or those with mixed alpha- and beta adrenoceptor properties such as adrenaline.

Administration to pregnant mothers shortly before giving birth or during labour may result in the newborn infants being born hypotonic, collapsed and hypoglycaemic.

Adverse effects are more likely to occur in patients with renal decompensation. Since BIO-ATENOLOL is excreted via the kidneys, dosage should be reduced in patients with a creatinine clearance of below 35 ml/min/1,73 m^2.

BIO-ATENOLOL may cause a more severe reaction to a variety of allergens when given to patients with a history of anaphylactic reaction to such allergens. Such patients may be unresponsive to the usual doses of adrenaline (epinephrine) used to treat the allergic reactions.

BIO-ATENOLOL may cause a hypersensitivity reaction including angioedema and urticaria.

Lactose warning

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take BIO ATENOLOL (see section 4.5).

Sodium content

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that it is to say essentially 'sodium-free'.

4.5 Interaction with other medicines and other forms of interaction

Combined use of beta-blockers and calcium channel blockers with negative inotropic effects, e.g., verapamil and diltiazem, can lead to an exaggeration of these effects particularly in patients with impaired ventricular function and/or sinoatrial or atrioventricular conduction abnormalities. This may result in severe hypotension, bradycardia and cardiac failure. Neither the beta-blocker nor the calcium channel blocker should be administered intravenously within 48 hours of discontinuing the other.

Concomitant therapy with dihydropyridines, e.g., nifedipine, may increase the risk of hypotension, and cardiac failure may occur in patients with latent cardiac insufficiency.

Digitalis glycosides, in association with beta-blockers, may increase atrioventricular conduction time.

Special note:

Digitalisation of patients receiving long term BIO-ATENOLOL therapy may be necessary if congestive cardiac failure is likely to develop. This combination can be considered despite the potentiation of 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 may exacerbate the rebound hypertension which can follow the withdrawal of clonidine. If the two medicines are co-administered, the beta-blocker should be withdrawn several days before discontinuing clonidine. If replacing clonidine by beta-blocker therapy, the introduction of beta-blockers should be delayed for several days after clonidine administration has stopped (refer to prescribing information for clonidine).

Class I anti-dysrhythmic medicine (e.g., disopyramide) and amiodarone may have a potentiating effect on atrial-conduction time and induce negative inotropic effect.

It can be dangerous to administer BIO-ATENOLOL concomitantly with the following medicine: phenothiazines. N.B. Such drug-drug interactions can have life-threatening consequences (see section 4.4).

Concomitant use of sympathomimetic medicines, e.g., adrenaline (epinephrine), may counteract the effect of beta-blockers.

Concomitant use with insulin and oral antidiabetic medicine may lead to the intensification of the blood sugar lowering effects of these medicines. Symptoms of hypoglycaemia, particularly tachycardia, may be masked (see section 4.4).

Concomitant use of prostaglandin synthetase-inhibiting medicine, e.g., ibuprofen and indomethacin, may decrease the hypotensive effects of beta-blockers.

Caution must be exercised when using anaesthetic medicines with BIO-ATENOLOL. The anaesthetist should be informed and the choice of anaesthetic should be a medicine with as little negative inotropic activity as possible. Use of beta-blockers with anaesthetic medicine may result in attenuation of the reflex tachycardia and increase the risk of hypotension. Anaesthetic medicines causing myocardial depression are best avoided.

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety and/or efficacy of BIO-ATENOLOL in women who are, or may become, pregnant has not been established, particularly in the first and second trimesters, since beta-blockers such as BIO-ATENOLOL, in general, have been associated with a decrease in placental perfusion which may result in intra-uterine deaths, immature and premature deliveries.

BIO-ATENOLOL crosses the placental barrier and appears in the cord blood. No studies have been performed on the use of BIO-ATENOLOL in the first trimester and the possibility of foetal injury cannot be excluded.

BIO-ATENOLOL has been used under close supervision for the treatment of hypertension in the third trimester. Administration of BIO-ATENOLOL to pregnant women in the management of mild to moderate hypertension has been associated with intra-uterine growth retardation.

Breastfeeding

There is significant accumulation of BIO-ATENOLOL in breast milk.

Neonates born to mothers who are receiving BIO-ATENOLOL at parturition or breastfeeding may be at risk of hypoglycaemia and bradycardia.

Caution should be exercised when BIO-ATENOLOL is administered during pregnancy or to a woman who is breastfeeding.

4.7 Effects on ability to drive and use machines

BIO-ATENOLOL has no or negligible influence on the ability to drive and use machines. However, dizziness and fatigue has been reported during treatment with BIO-ATENOLOL. Patients should not drive or use machines until they have determined how they are affected.

4.8 Undesirable effects

MedDRA System organ class	**Frequency**	**Undesirable Effect**
Blood and lymphatic system disorders	*Less frequent*	Purpura, thrombocytopenia.
Psychiatric disorders	*Less frequent*	Sleep disturbances of the type noted with other beta-blockers, mood changes, depression, nightmares, vivid dreams, confusion, psychoses and hallucinations, depression and malaise.
Nervous system disorders	*Less frequent*	Dizziness, headache, paraesthesia.
Eye disorders	*Less frequent*	Dry eyes, visual disturbances.
Cardiac disorders	*Frequent*	Congestive cardiac failure, marked bradycardia.
	Less frequent	Heart failure deterioration, precipitation of heart block.
Vascular disorders	*Frequent*	Cold extremities.
	Less frequent	Postural hypotension which may be associated with syncope, intermittent claudication may

		be increased if already present, in susceptible patients Raynaud's phenomenon (due to unopposed arteriolar alpha-sympathetic activation).
Respiratory, thoracic and mediastinal disorders	*Less frequent*	Bronchospasm may occur in patients with bronchial asthma or a history of asthmatic complaints.
Gastrointestinal disorders	*Frequent*	Gastrointestinal disturbances, nausea, vomiting, diarrhoea.
	Less frequent	Dry mouth.
Hepato-biliary disorders	*Less frequent*	Elevations of transaminase levels, hepatic toxicity including intrahepatic cholestasis.
Skin and subcutaneous tissue disorders	*Less frequent*	Alopecia, psoriasiform skin reactions, exacerbation of psoriasis, skin rashes.
	Frequency not known	Hypersensitivity reactions, including angioedema and urticaria.
Discontinuation of the medicine should be considered if any such reaction is not otherwise explicable.		
Musculoskeletal and connective tissue disorders	*Frequency not known*	Lupus-like syndrome.
Reproductive system and breast disorders	*Less frequent*	Impotence.
General disorders and administration site conditions	*Frequent*	Fatigue.
Investigations	*Less frequent*	An increase in ANA (Antinuclear Antibodies) has been observed, however the clinical relevance of this is not clear.

Adverse reactions are more frequent in patients with renal decompensation.

Discontinuance of the medicine should be considered if, according to clinical judgement, the well-being of the patient is adversely affected by any of the above reactions.

Side effects may be minimised by starting treatment with a small dose and gradually increasing it.

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 Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

Intensive care may be required for several days since the effect of beta-adrenoceptor blocking medicines last longer than their plasma half-life.

Overdosage may produce bradycardia, and severe hypotension. Bronchospasm and heart failure may be produced in certain individuals. Cases of mild overdose should be observed for at least four hours, as apnoea and cardiovascular collapse may appear suddenly. Repeated activated charcoal is necessary in severe overdose.

Atropine may be used to treat severe bradycardia. If the response is inadequate, glucagon may be given intravenously. Alternatively, dobutamine or isoprenaline, may be required to reverse beta-blockade. Intravenous cardiac pacing may be required for severe bradycardia. Bronchospasm should be treated with IV aminophylline or inhaled, or IV beta-agonist, e.g., salbutamol.

Atropine should be given intravenously in divided doses to reduce unopposed vagal activity. Isoprenaline

should be given by infusion according to the response of the pulse and blood pressure, massive doses may be required. Bronchospasm may be treated by intravenous aminophylline and heart failure with digitalis and diuretics.

5 PHARMACOLOGICAL PROPERTIES

Category and class: A 5.2 Adrenolytics (sympathicolytics)

Pharmacotherapeutic group: Beta-blocking agents, plain, selective, ATC code: CO7A B03.

5.1 Pharmacodynamic properties

BIO-ATENOLOL is a selective beta-adrenergic blocking agent with insignificant partial agonist activity and weak membrane-stabilizing properties.

5.2 Pharmacokinetic properties

It is incompletely absorbed after oral administration and is excreted largely in the urine. It has a plasma half-life of approximately 6-8 hours, but its anti-hypertensive
effects appears to last considerably longer. It may thus be administered in a once daily dosage for the treatment of hypertension.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Croscarmellose sodium type A

Lactose monohydrate

Maize starch

Magnesium stearate

Povidone

Pregelatinised maize starch

Opadry orange (consisting of hypromellose; titanium dioxide, hydroxypropyl cellulose, polyethylene glycol, sunset yellow FCF aluminium lake and talc).

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 and moisture.

6.5 Nature and contents of container

BIO-ATENOLOL 50: Packs of 28 and 30 tablets, packed into securitainers or PVC/PVDC/Alu blisters.

BIO-ATENOLOL 100: Packs of 28 and 30 tablets, packed into securitainers or PVC/PVDC/Alu blisters.

6.6 Special precautions for disposal and other handling

No special requirements

7 HOLDER OF CERTIFICATE OF REGISTRATION

Biotech Laboratories (Pty) Ltd

Ground Floor, Block K West, Central Park

400 16th Road, Randjespark

Midrand, 1685

8 REGISTRATION NUMBER(S)

BIO-ATENOLOL 50: W/5.2/0439

BIO-ATENOLOL 100: W/5.2/0440

9 DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

Date of registration: 22 Augustus 1991

10 DATE OF REVISION OF THE TEXT

05 May 2026.