Professional Information

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

B-BLOCK 50

B-BLOCK 100

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each **B-BLOCK 50** tablet contains 50 mg atenolol.

Sugar free.

Each **B-BLOCK 100** tablet contains 100 mg atenolol.

Sugar free.

For full list of excipients, see **section 6.1**

3. PHARMACEUTICAL FORM

B-BLOCK 50:

White, round shaped, biconvex, film-coated tablets, plain on both sides.

B-BLOCK 100:

Orange coloured, round, biconvex, film-coated tablets with a

breakline on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Management of angina pectoris and hypertension.

Myocardial infarction, early intervention in the acute phase.

4.2 Posology and method of administration

Posology

Adults:

Angina Pectoris:

Most patients with angina pectoris will respond to a dose of 100 mg daily. This is most conveniently administered as a single 100 mg tablet once daily, which may if desired be given in the form of one 50 mg tablet twice daily. It is unlikely that additional benefit will be obtained by increasing the dose.

Hypertension:

Most patients will respond with a fall in blood pressure to a dose of 100 mg once daily. This is most conveniently administered as a single 100 mg tablet once daily. It is unlikely that additional benefit will be gained by increasing the dosage. In refractory cases a further reduction of blood pressure may be achieved by combining **B-BLOCK** with other antihypertensive agents. **B-BLOCK** is compatible with diuretics and other hypotensive agents. For example, co-administration of **B-BLOCK** with a diuretic provides a highly effective antihypertensive therapy. Patients can be transferred to **B-BLOCK** from other antihypertensive treatment.

Special Populations:

Renal failure:

Since **B-BLOCK** is excreted via the kidneys dosage should be adjusted in cases of severe impairment of renal function. No significant accumulation of B-BLOCK 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/1,73 m^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 m2 (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 **B-BLOCK** and for this reason it is not recommended for use in children.

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.

Method of administration

B-BLOCK is for oral administration.

4.3 Contraindications

B-BLOCK is contraindicated:

- In patients with known hypersensitivity to atenolol or any of its excipients listed in section 6.1
- In pregnancy and lactation
- In the presence of second degree or third-degree heart block
- With verapamil; and neither medicine should be administered within several days of discontinuing the other
- After prolonged fasting
- In patients with metabolic acidosis (e.g. diabetes)
- In cardiac failure, unless or until signs of failure are controlled with digitalis and/or diuretics
- Uncontrolled cardiac failure, excluding that due to hypertrophic obstructive cardiomyopathy

- **B-BLOCK** should not be used in patients with cardiogenic shock

Particular caution should be exercised with patients suffering from the following: asthma, bronchitis, chronic respiratory diseases, second and third degree heart block and bradycardia (less than 50 beats per minute), peripheral vascular diseases and Raynaud's phenomenon. The normal dose should be reduced in elderly patients, or in patients suffering from renal dysfunction. 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."

4.4 Special warnings and precautions for use

While taking **B-BLOCK**, patients with a history of anaphylactic reactions to a variety of allergens, may have a more severe reaction on repeated challenge. Such patients may be unresponsive to the usual dose of adrenaline used to treat allergic reactions.

Particular caution should be exercised with patients suffering from the following:

Bradycardia of less than 50 pulse beats per minute, peripheral vascular disease and Raynaud's phenomenon.

The normal dose should be reduced in elderly patients, or in patients suffering from renal dysfunction. Elderly patients may not respond as well to atenolol as younger patients.

In the perioperative 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 of 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.

Caution should be exercised when transferring a patient from clonidine. The withdrawal of clonidine may result in the release of large amounts of catecholamines which may give rise to a hypertensive crisis. If beta-blockers are administered in these circumstances, the unopposed alpha-receptor stimulation may potentiate this effect. If a beta-blocker and clonidine are given concurrently, the clonidine should not be discontinued until several days after the withdrawal of the beta-blocker, as severe rebound hypertension may occur.

Bronchoconstriction may occur in patients suffering from asthma, bronchitis and other chronic pulmonary diseases. Congestive cardiac failure and marked bradycardia may ~~occur.~~ also manifest. A variety of neuropsychiatric disorders, ranging from vague fatigue and nightmares to overt psychosis, have been observed.
The following may occur: exacerbation of peripheral vascular disease, or the development of Raynaud's phenomenon (due to unopposed arteriolar alpha-sympathetic activation), 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 drug intravenously.

It is dangerous to administer this medicine concomitantly with the following medicines: hypoglycaemic agents, phenothiazines and various antiarrhythmic agents. Such drug-drug interactions can have life-threatening consequences.

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.

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.

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

Patients with phaeochromocytoma usually require treatment with an alpha-adrenergic blocker.

B-BLOCK may mask the symptoms of hyperthyroidism.

B-BLOCK may unmask myasthenia gravis.

Psoriasis may be aggravated.

Care should be taken in prescribing a Class 1 antidysrhythmic agent such as disopyramide. Beta-adrenoceptor blocking agents should be used with caution in combination with verapamil in patients with impaired ventricular function. The combination should not be given to patients with conduction abnormalities. Caution should be exercised when transferring patients from clonidine to beta-adrenoceptor blocking agents. If beta-adrenoceptor blocking agents and clonidine are given concurrently, clonidine should not be discontinued until several days after withdrawal of the beta-adrenoceptor blocking agent (also see prescribing information for clonidine).

There have been reports of skin rashes and/or dry eyes associated with the use of **B-BLOCK**. Discontinuation of the medicine should be considered if any such reaction is not otherwise explicable.

Anaesthesia:

It may be decided to withdraw **B-BLOCK** before surgery. In this case 48 hours should be allowed to elapse from the last dose and anaesthesia. If treatment is continued, anaesthetic agents causing myocardial depression, such as ether, cyclopropane, and trichloroethylene are best avoided. Vagal

dominance, if it occurs, may be corrected with atropine (1-2 mg iv).

B-BLOCK contains propylene glycol which has not been shown to cause reproductive or developmental toxicity in animals or humans, it may reach the foetus and was found in milk. As a consequence, administration of propylene glycol to pregnant or lactating patients should be considered on a case by case basis.

Medical monitoring is required in patients with impaired renal or hepatic functions because various adverse events attributed to propylene glycol have been reported such as renal dysfunction (acute tubular necrosis), acute renal failure and liver dysfunction.

Various adverse events, such as hyperosmolality, lactic acidosis; renal dysfunction (acute tubular necrosis), acute renal failure; cardiotoxicity (arrhythmia, hypotension); central nervous system disorders (depression, coma, seizures); respiratory depression, dyspnoea; liver dysfunction; haemolytic reaction (intravascular haemolysis) and haemoglobinuria; or multisystem organ dysfunction, have been reported with high doses or prolonged use of propylene glycol. Therefore doses higher than 500 mg/kg/day may be administered in children > 5 years old but will have to be considered case by case. Adverse events usually reverse following weaning off of propylene glycol, and in more severe cases following hemodialysis. Medical monitoring is required.

4.5 Interaction with other medicines and other forms of interaction

Use of **B-BLOCK** with anaesthetic agents may increase the risk of myocardial depression and hypotension. Anaesthetics causing myocardial depression, such as ether, cyclopropane, and trichloroethylene, are best avoided and anaesthetists should be informed that **B-BLOCK** is being taken.

It can be dangerous to administer this medicine concomitantly with the following medicines:

Hypoglycaemic agents, phenothiazines and various antiarrhythmic agents.

NB: Such interactions can have life-threatening consequences.

Special note:

Digitalization of patients receiving long-term **B-BLOCK** 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.

Combined use of **B-BLOCK** and calcium channel blockers with negative inotropic effects, e.g. verapamil and diltiazem, can lead to exaggeration of these effects, particularly in patients with impaired ventricular function and/or SA or AV conduction abnormalities. Neither medicine should be administered intravenously within 48 hours of discontinuing the other.

Heart failure and severe hypotension have been reported in combination with nifedipine.

Concomitant use of prostaglandin synthetase inhibiting drugs, e.g. ibuprofen and indomethacin, may decrease the hypotensive effect of **B-BLOCK**.

Concomitant use of sympathomimetic agents, e.g. adrenaline, may counteract the effect of **B-BLOCK**.

4.6 Fertility, pregnancy and lactation

B-BLOCK is contra-indicated in pregnancy and lactation.

Pregnancy

B-BLOCK crosses the placental barrier and appears in cord blood. Administration to pregnant women has been associated with intra-uterine growth retardation.

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

Breastfeeding

There is significant accumulation in breast milk. Breastfeeding patients must not take **B-BLOCK.**

4.7 Effects on ability to drive and use machines

Use is unlikely to result in any impairment of the ability of patients to drive or operate machinery. However, it should be taken into account that occasionally dizziness or fatigue may occur.

4.8 Undesirable effects

System organ class	Frequency	Adverse reaction
Blood and lymphatic system disorders	Less frequently	Nonthrombocytopenic purpura, Agranulocytosis
	Rarely	Thrombocytopenia, transient eosinophilia
Immune system disorders	Rare	Lupus-like syndrome
Metabolism and nutrition disorders	Rare	B-BLOCK interferes with carbohydrate and lipid metabolism and can produce hypoglycaemia, hyperglycaemia and changes in blood concentrations of triglycerides and cholesterol.

Psychiatric disorders	Frequent	Sleep disturbances (insomnia) unusual tiredness or weakness (fatigue) and drowsiness.
	Less frequent	Depression
	Rare	Confusion, nightmares, vivid dreams, hallucinations, overt psychosis. Coma and convulsions have been reported following overdosage.
Nervous system disorders	Rare	Paraesthesia, peripheral neuropathy, myopathies including muscle cramps, dizziness, lassitude
Eye disorders	Rare	Decreased tear production, blurred vision, and soreness
Cardiovascular disorders	Less frequent	Congestive heart failure, bradycardia, hypotension Heart failure or heart block may be precipitated in patients with underlying cardiac disorders.
Vascular disorders	Less frequent	Reduced peripheral circulation can produce coldness of the extremities and may exacerbate peripheral vascular disease such as Raynaud's syndrome

Respiratory, thoracic and mediastinal disorders	Less frequent	Bronchospasm may be precipitated in susceptible patients with bronchial asthma or a history of asthmatic complaints
	Rare	pneumonitis, pulmonary fibrosis
Gastrointestinal disorders	Less frequent	Nausea, vomiting, diarrhoea, constipation and abdominal cramps
	Rare	Sclerosing peritonitis, retroperitoneal fibrosis
Skin and subcutaneous tissue disorders	Rare	Skin rash, reversible alopecia, and pruritus
Musculoskeletal and connective tissue disorders	Rare	Muscular fatigue, malaise, myopathies including muscle cramps
Reproductive system and breast disorders	Rare	Male impotence

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

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 4 hours, as apnoea and cardiovascular collapse may appear suddenly.

Repeated activated charcoal is necessary in severe overdoses.

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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A.5.2 Adrenolytics (Sympathicolytics)

ATC CODE: C07AB03

B-BLOCK is a beta-adrenoreceptor blocking agent which acts preferentially on beta-adrenergic receptors in the heart. It has no intrinsic sympathomimetic or membrane stabilizing activity. Human studies indicate that it crosses the blood-brain barrier only to a negligible extent. The mode of action in the treatment of hypertensions is unclear. It is probably the reduction in cardiac rate and contractility which makes it effective in eliminating or reducing the symptoms of patients with angina.

5.2 Pharmacokinetic properties

Absorption of atenolol following oral dosing is consistent but incomplete (approximately 40 – 50 %) with peak plasma concentrations occurring 2 - 4 hours after dosing. There is no significant hepatic

metabolism of atenolol and more than 90 % of that absorbed reaches the systemic circulation unaltered. The plasma half-life is about 6 hours but this may rise in severe renal impairment since the kidney is the major route of elimination. Atenolol penetrates tissues poorly due to its low lipid solubility and its concentration in brain tissue is low. Plasma protein binding is low (approximately 3 %).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet Core

- Magnesium Stearate
- Maize Starch
- Microcrystalline cellulose
- Purified Water
- Sodium Lauryl Sulphate
- Sodium Starch Glycolate

Coating

- Dichloromethane
- Ethyl Cellulose (20 cps)
- Hydroxy propyl methyl cellulose (5 cps)
- Isopropyl Alcohol
- Polyethyene Glycol 400
- Propylene Glycol
- Purified Talc
- Titanium Dioxide
- Sunset yellow lake colour (CI No. 15985) (B-BLOCK 100)

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25 ºC. Protect from light and moisture.

6.5 Nature and contents of container

B-BLOCK 50:

Cartons containing 10 aluminium foil strip packs of 10 tablets each. i.e. 100 tablets per carton.

Cartons containing 10 blister packs of 10 tablets each. i.e. 100 tablets per carton.

Cartons containing 3 blister packs of 10 tablets each. i.e. 30 tablets per carton.

B-BLOCK 100:

Cartons containing 10 blister packs of 10 tablets each. i.e. 100 tablets per carton.

Cartons containing 3 blister packs of 10 tablets each. i.e. 30 tablets per carton.

6.6 Special precautions for disposal <and other handling

Not Applicable

7 HOLDER OF CERTIFICATE OF REGISTRATION

RANBAXY PHARMACEUTICALS (PTY) LTD

14 LAUTRE ROAD

STORMILL

EXT. 1

ROODEPOORT

1724 SOUTH AFRICA

8 REGISTRATION NUMBER(S)

B-BLOCK 50: 31/5.2/0332 (S.A.)

B-BLOCK 100: 32/5.2/0670 (S.A.)

B-BLOCK 50: S2 BOT 0801395 (Botswana)

B-BLOCK 100: S2 BOT 0801396 (Botswana)

B-BLOCK 50: 07/5.2/0073 (Namibia)

B-BLOCK 100: 07/5.2/0074 (Namibia)

9 DATE OF FIRST AUTHORISATION

11 February 2005

10 DATE OF REVISION OF THE TEXT

23 December 2022