## Professional Information

**Scheduling status** **S3**

### 1. NAME OF THE MEDICINAL PRODUCT

HEXA-BLOK 50 (film-coated tablets)

HEXA-BLOK 100 (film-coated tablets)

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Hexa-Blok 50 film-coated tablet contains atenolol 50 mg.

Each Hexa-Blok 100 film-coated tablet contains atenolol 100 mg.

**Hexa-block contains sugar**

Each Hexa-Blok 50 film-coated tablet contains 2,88 mg lactose monohydrate.

Each Hexa-Blok 100 film-coated tablet contains 4,32 mg lactose monohydrate.

For the full list of excipients, see section 6.1.

### 3. PHARMACEUTICAL FORM

Hexa-Blok 50: White, round and biconvex film-coated tablet, intact surface, with one-sided score notch and embossment “50” on the other side.

Hexa-Blok 100: White, round and biconvex film-coated tablet, intact surface, with one-sided score notch and embossment “100” on the other side.

### 4. CLINICAL PARTICULARS

**4.1 Therapeutic indications**

Management of angina pectoris and hypertension.

**4.2 Posology and method of administration**

Hexa-Blok is compatible with diuretics and other hypotensive medicines.

**Angina pectoris**

The usual dose is 50 to 100 mg daily given as single or divided doses.

Additional benefit is not usually obtained from higher doses of atenolol.

**Hypertension**

The initial dose for the treatment of hypertension is usually 50 mg per day given once daily. If an adequate therapeutic response is not evident within several weeks the daily dose may be increased to 100 mg. Higher doses are unlikely to provide any greater anti-hypertensive effect.

In refractory cases a further reduction of blood pressure may be achieved by combining Hexa-Blok with other anti-hypertensive agents for example co-administration of Hexa-Blok with a diuretic.

**4.3 Contraindications**

**Hexa-Blok is contraindicated in:**

- Known hypersensitivity to the active substance or any of the excipients included in Hexa-Blok.
- Cardiogenic shock.
- Sick sinus syndrome.
- Second and third degree heart block.
- Untreated pheochromocytoma.
- Metabolic acidosis.
- Uncontrolled heart failure.
- Bradycardia (< 45 bpm).
- Hypotension.
- Severe peripheral arterial circulatory disturbances.

Particular caution should be exercised with patients suffering from the following: asthma, bronchitis, chronic respiratory 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 of Hexa-Blok therapy 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 by beta-blocker therapy. Particular caution should be taken in this regard.

**4.4 Special warnings and precautions for use**

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 such as Hexa-Blok are administered in these circumstances the unopposed alpha receptor stimulation may potentiate this effect.

If a beta-blocker such as Hexa-Blok and clonidine are given concurrently, the clonidine should not be discontinued until several days after withdrawal of the beta-blocker as severe rebound hypertension may occur (see section 4.5).

**The following may occur:**

Exacerbation of peripheral vascular diseases, or the development of Raynaud's phenomenon (due to unopposed arteriolar alpha-sympathetic activation), sexual impotence, hypoglycaemia, skeletal muscle weakness and gastrointestinal 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 Hexa-Blok intravenously.

Although contraindicated in severe peripheral arterial circulatory disturbances (see section 4.3). Hexa-Blok may also aggravate less severe peripheral arterial circulatory disturbances.

Since atenolol is excreted via the kidneys, the normal dose of Hexa-Blok should be reduced in patients with a creatinine clearance of below 35 mℓ/min/1,73 $m^2$.

Hexa-Blok should be used with caution in the elderly, starting with a lesser dose.

When a patient is scheduled for surgery, and a decision is made to discontinue Hexa-Blok therapy, this should be done at least 24 hours prior to the procedure. The risk-benefit assessment of stopping beta- blockage should be made for each patient. If treatment is continued, an 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.

Hexa-Blok should not be withdrawn abruptly. Abrupt discontinuation of therapy may cause exacerbation of angina pectoris in patients suffering from ischaemic heart disease. The dosage should be withdrawn gradually over a period of 7 – 14 days, to facilitate a reduction in beta-blocker dosage. Patients should be advised to limit the extent of their physical activity during the period that Hexa-Blok is being discontinued. Patients should be followed during withdrawal, especially those with ischaemic heart disease.

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

Hexa-Blok may increase the number and duration of angina attacks in patients with Prinzmetal's angina due to unopposed alpha-receptor mediated coronary artery vasoconstriction. Atenolol, as

contained in Hexa-Blok, is a beta1-selective beta-blocker; 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 Hexa-Blok is given to patients with first-degree heart block.

Hexa-Blok may mask the symptoms of hypoglycaemia, in particular, tachycardia.

Hexa-Blok may mask the signs of thyrotoxicosis.

Hexa-Blok 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.

Hexa-Blok 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.

Bronchoconstriction may occur in patients suffering from asthma, bronchitis and other chronic pulmonary diseases when Hexa-Blok is administered. Congestive cardiac failure and marked bradycardia may also manifest. A variety of neuropsychiatric disorders, ranging from vague fatigue and nightmares to overt psychosis, have been observed.
Hexa-Blok may cause and increase in airways resistance in asthmatic patients. Hexa-Blok is a beta1-selective beta-blocker; consequently its use may be considered although utmost caution must be exercised. If increased airways resistance does occur, Hexa-Blok should be discontinued and bronchodilator therapy (e.g., salbutamol administered if necessary.

Hexa-Blok should only be given to patients with psoriasis after careful consideration, as psoriasis may be aggravated.

As with other beta-blockers, in patients with a pheochromocytoma, an alpha-blocker should be given concomitantly to Hexa-Blok therapy.

It is dangerous to administer Hexa-Blok concomitantly with the following medicines: hypoglycaemic medicines, phenotiazines and various antidysrhythmic medicines. Such medicine-medicine interactions can have life-threatening consequences (see section 4.5).

Administration to pregnant mothers shortly before giving birth or during labour may result in the newborn infants being born hypnotic, collapsed and hypoglycaemic (see section 4.6).

**Special note:** Digitalization 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 negative chronotropic effects of the two medicines. Careful control of dosages and of the individual patient's response (and notably pulse rate) is essential in this situation.

**4.5 Interaction with other medicines and other forms of interaction**

Combined use of beta-blockers such as Hexa-Blok 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 such as Hexa-Blok 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 such as Hexa-Blok, may increase atrioventricular conduction time.

Beta-blockers such as Hexa-Blok 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 Hexa-Blok therapy, the introduction of Hexa-Blok should be delayed for several days after clonidine administration has stopped.

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

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

Concomitant use with insulin and oral anti-diabetic medicines 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 medicines, e.g., ibuprofen and indometacin, may decrease the hypotensive effects of Hexa-Blok

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

Concomitant use of baclofen may increase the antihypertensive effect making dose adjustments necessary

**4.6 Fertility, pregnancy, and lactation**

**Pregnancy**

Atenolol crosses the placental barrier and appears in the cord blood. No studies have been performed on the use of Hexa-Blok in the first trimester and the possibility of foetal injury cannot be excluded. Hexa-Blok has been used under close supervision for the treatment of hypertension in the third trimester. Administration of Hexa-Blok to pregnant women in the management of mild to moderate hypertension has been associated with intra-uterine growth retardation.

The use of Hexa-Blok in women who are, or may become, pregnant requires that the anticipated benefit be weighed against the possible risks, particularly in the first and second trimesters, since beta-blockers such as Hexa-Blok, in general, have been associated with a decrease in placental perfusion which may result in intra-uterine deaths, immature and premature deliveries.

**Lactation**

There is significant accumulation of atenolol in breast milk.
Neonates born to mothers who are receiving Hexa-Blok at parturition or breast-feeding may be at risk of hypoglycaemia and bradycardia.

Caution should be exercised when Hexa-Blok is administered during pregnancy or to a woman who is breast-feeding.

**4.7 Effects on ability to drive and use machines**

Hexa-Blok 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.

**Important information about some excipients**

Hexa-Blok contains lactose monohydrate. Patients with the rare hereditary conditions of galactose intolerance e.g. galactosaemia, Lapp lactase deficiency, glucose-galactose malabsorption or fructose intolerance should not take Hexa-Blok.

Hexa-Blok contains lactose monohydrate, which may have an effect on the glycaemic control of patients with diabetes mellitus.

**4.8 Undesirable effects**

**Blood and lymphatic system disorders**

*Less frequent:* Purpura, thrombocytopenia.

**Psychiatric disorders**

*Less frequent:* Sleep disturbances, mood changes, nightmares, confusion, psychoses and hallucinations.

**Nervous system disorders**

*Less frequent:* Dizziness, headache, paraesthesia.

**Eye disorders**

*Less frequent:* Dry eyes, visual disturbances.

**Cardiac disorders**

*Frequent:* 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.

**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.

*Less frequent*: Dry mouth.

*Frequency not known:* Constipation.

**Hepatobiliary disorders**

*Less frequent:* Elevation 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.

**Musculoskeletal and connective tissue disorders**

*Frequency not known:* Lupus-like syndrome

**Reproductive system and breast disorders**

*Less frequent:* Impotence, libido disorder

**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.

**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.

**4.9 Overdose**

The symptoms of overdosage with Hexa-Blok may include bradycardia, hypotension, acute cardiac insufficiency and bronchospasm.

**General treatment should include:** close supervision; treatment in an intensive care ward; the use of gastric lavage; activated charcoal and a laxative to prevent absorption of any medicine still present in the gastrointestinal tract; the use of plasma or plasma substitutes to treat hypotension and shock. The possible uses of haemodialysis or haemoperfusion may be considered.

Excessive bradycardia can be countered with atropine 1 – 2 mg intravenously and/or a cardiac pacemaker. If necessary, this may be followed by a bolus dose of glucagon 10 mg intravenously. If required, this may be repeated or followed by an intravenous infusion of glucagon 1–10 mg/hour depending on response. If no response to glucagon occurs or if glucagon is unavailable, a beta-adrenoceptor stimulant such as dobutamine 2,5 to 10 micrograms/kg/minute by intravenous infusion may be given. Dobutamine, because of its positive inotropic effect could also be used to treat hypotension and acute cardiac insufficiency. It is likely that these doses would be inadequate to reverse the cardiac effects of beta-blockade if a large overdose has been taken. The dose of

dobutamine should therefore be increased if necessary, to achieve the required response according to the clinical condition of the patient.

Bronchospasm can usually be reversed by bronchodilators and should be treated with IV aminophylline or inhaled, or IV beta-agonist, e.g. salbutamol.

## 5. PHARMACOLOGICAL PROPERTIES

A 5.2 Adrenolytics (Sympathicolytics)

Pharmacotherapeutic group: Beta-blocking agents, plain, selective**,** ATC code: C07A B03**.**

### 5.1 Pharmacodynamic properties

Hexa-Blok is a beta-adrenoreceptor blocking medicine which acts preferentially on beta-adrenergic receptors in the heart. It has no intrinsic sympathomimetic or membrane stabilising activity. Hexa-Blok (atenolol) is very hydrophilic and appears to penetrate the brain to only a limited extent.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Hexa-Blok 50 and 100: Hydroxypropylcellulose, magnesium carbonate (heavy), magnesium stearate, maize starch, sodium dodecyl sulphate, sodium starch glycollate, Opadry white (consists of lactose monohydrate, methylhydroxypropylcellulose, polyethylene glycol 4000 and titanium dioxide)

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

48 months

### 6.4 Special precautions for storage

Store in a dry place at or below 25 °C.

Protect from light. Keep blisters in carton until required for use.

**KEEP OUT OF THE REACH OF CHILDREN.**

### 6.5 Nature and contents of container

Hexa-Blok 50: PVC/PE/PVDC/Aluminium blister packs, containing 30 tablets

Hexa-Blok 100: PVC/PE/PVDC/Aluminium blister packs, containing 30 tablets

### 6.6 Special precautions for disposal and other handling

No special requirements.

## 7. HOLDER OF CERTIFICATE OF REGISTRATION

Sandoz SA (Pty) Ltd[1]

Waterfall 5-lr

Magwa Crescent West

Waterfall City

Jukskei View

2090

## 8. REGISTRATION NUMBER(S)

Hexa-Blok 50:  27/5.2/0468

Hexa-Blok 100:  27/5.2/0469

## 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

11 October 1993

## 10. DATE OF REVISION OF THE TEXT

27 May 2022

[1] Company Reg. No.: 1990/001979/07