PROFESSIONAL INFORMATION

SCHEDULING STATUS S3

1 NAME OF THE MEDICINE

SOTAHEXAL 80 (tablets)

SOTAHEXAL 160 (tablets)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

SotaHexal 80: Each tablet contains 80 mg sotalol hydrochloride.

SotaHexal 160: Each tablet contains 160 mg sotalol hydrochloride.

Excipients

SotaHexal 80 tablets contains sugar (26,75 mg lactose monohydrate).

SotaHexal 160 tablets contains sugar (53,5 mg lactose monohydrate).

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Tablets

SotaHexal 80: White, round tablets, scored on one side, convex with “SOT” embossed on the other side.

6,9 to 7,1 mm (Diameter); 2,8 to 3,2 mm (Height).

SotaHexal 160: White, round biconvex tablets. Scored on one side with “SOT” imprint on the other side.

8,9 to 9,1 mm (Diameter); 3,8 to 4,2 mm (Height)

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

SOTAHEXAL is indicated in the management of hypertension, angina pectoris and cardiac dysrhythmias. SOTAHEXAL has been given following myocardial infarction to prevent re-infarction and in addition has been given to reduce symptoms of sympathetic overactivity in hyperthyroidism.

4.2 Posology and method of administration

Hypertension:

Initial oral dose 160 mg daily as a single or divided dose, which may be increased at fortnightly intervals according to the response of the patient to 600 mg or more daily.

Angina pectoris:

Optimum dose between 160 mg and 600 mg daily.

Cardiac dysrhythmias:

120 mg to 480 mg daily.

Post MI to prevent re-infarction:

320 mg daily.

Hyperthyroidism to reduce symptoms of sympathetic overactivity:

120 to 240 mg daily.

Reduced doses may be required in renal impairment, hepatic dysfunction and in the elderly.

4.3 Contraindications

- Hypersensitivity to sotalol hydrochloride or any of the other ingredients of SOTAHEXAL.
- Evidence of sick sinus syndrome, including sino-atrial block, unless a functioning pacemaker is present.
- Second and third degree AV heart block unless a functioning pacemaker is present.
- Congenital or acquired long QT syndromes or medicines associated with possible QT interval prolongation (see section 4.5)
- Torsade de pointes or medicines associated with it (see section 4.5).
- Symptomatic sinus bradycardia (≤ 45 to 50 bpm).
- Uncontrolled congestive heart failure, including congestive heart failure of the right ventricle after pulmonary hypertension.
- Cardiogenic shock.
- Untreated phaeochromocytoma.
- Anaesthesia that produces myocardial depression.
- Hypotension (except due to dysrhythmia).
- Raynaud's phenomenon and severe peripheral circulatory disturbances.
- Asthma, bronchitis or a history of obstructive airway disease.
- Metabolic acidosis.
- Renal failure (creatinine clearance < 10 mℓ/min). 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 SOTAHEXAL 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.

- Pregnancy and lactation, unless a safer option is not available (see section 4.6).

4.4 Special warnings and precautions for use

Abrupt withdrawal:

Hypersensitivity to catecholamines is observed in patients withdrawn from beta-blocker therapy such as SOTAHEXAL. Occasional cases of exacerbation of angina pectoris, dysrhythmias, and in some cases, myocardial infarction have been reported after abrupt discontinuation of therapy. It is therefore advised that patients are carefully monitored when discontinuing chronically administered SOTAHEXAL, particularly those with ischaemic heart disease. If possible the dose should be gradually reduced over a period of one or two weeks. If necessary at the same time initiating replacement therapy. Abrupt discontinuation may unmask latent coronary insufficiency. In addition, hypertension may develop.

Pro-dysrhythmias:

The most dangerous adverse effect of anti-dysrhythmic medicines such as SOTAHEXAL is the aggravation of pre-existing dysrhythmias or the provocation of new dysrhythmias. Medicines that prolong the QT-interval may cause torsade de pointes, a polymorphic ventricular tachycardia associated with prolongation of the QT-interval. Experience to date indicates that the risk of torsade de pointes is associated with the prolongation of the QT-interval, reduction of the heart rate, reduction in serum potassium and magnesium, high plasma sotalol concentrations and with the concomitant use of SOTAHEXAL and other medications which have been associated with torsade de pointes. Females may be at increased risk of developing torsade de pointes.

The incidence of torsade de pointes is dose dependent. Torsade de pointes usually occur early after initiating therapy or escalation of the dose and can progress to ventricular fibrillation.

There have been reports that in patients with sustained VT/VF the incidence of severe pro-dysrhythmia (torsade de pointes or new sustained VT/VF) was < 2 % at doses up to 320 mg. The incidence more than doubled at higher doses.

Other risk factors for torsade de pointes were excessive prolongation of the QTc interval and history of cardiomegaly or congestive heart failure. Patients with sustained ventricular tachycardia and a history of congestive heart failure have the highest risk of serious pro-dysrhythmia (7 %).

Pro-dysrhythmic events must be anticipated not only on initiating therapy, but with every upwards dose adjustment. Initiating therapy at 80 mg with gradual upward dose titration thereafter reduces the risk of pro-dysrhythmia. SOTAHEXAL should be used with strict caution if the QTc interval exceeds 480 msec and serious consideration should be given to reducing the dose or discontinuing therapy when the QTC- interval exceeds 550 msec. Due to the multiple risk factors associated with the origination of torsade de pointes, however, caution should be exercised regardless of the QTc-interval duration.

Electrolyte disturbances:

SOTAHEXAL should not be used in patients with hypokalaemia or hypomagnesaemia prior to correction of imbalance; these conditions can exaggerate the degree of QT prolongation, and increase the potential for torsade de pointes. Special attention should be given to electrolyte and acid-base balance in patients experiencing severe or prolonged diarrhoea or patients receiving concomitant magnesium- and/or potassium-depleting medicines.

Congestive heart failure:

Beta-blockade produced by SOTAHEXAL may further depress myocardial contractility and precipitate more severe heart failure. Caution is advised when initiating therapy in patients with left ventricular dysfunction controlled by therapy (i.e. ACE inhibitors, diuretics, digoxin, etc.); a low initial dose and careful dose titration is appropriate.

Recent myocardial infarction:

In post-infarction patients with impaired left ventricular function, careful monitoring and dose titration are critical during initiation and follow-up of therapy. SOTAHEXAL should be avoided in patients with left ventricular ejection fractions ≤ 40 % without serious ventricular dysrhythmias.

Electrocardiographic changes:

Excessive prolongation of the QT-interval, > 500 msec, can be a sign of toxicity and should be avoided. Sinus bradycardia has been observed very commonly in dysrhythmia patients receiving SOTAHEXAL. Bradycardia increases the risk of torsade de pointes. Sinus pause, sinus arrest and sinus node dysfunction occur in less than 1 % of patients. The incidence of 2nd or 3rd degree AV block is approximately 1 %.

Anaphylaxis:

Patients with a history of anaphylactic reaction to a variety of allergens may have a more severe reaction on repeated challenge while taking beta-blockers such as SOTAHEXAL. Such patients may be unresponsive to the usual doses of epinephrine (adrenaline) used to treat the allergic reaction.

Anaesthesia:

SOTAHEXAL should be used with caution in patients undergoing surgery and where anaesthetics that cause myocardial depression, such as cyclopropane or trichloroethylene are used (see section 4.3).

Diabetes mellitus:

SOTAHEXAL should be used with caution in patients with diabetes (especially labile diabetes) or with a history of episodes of spontaneous hypoglycaemia, since beta-blockade may mask some important signs of the onset of acute hypoglycaemia e.g. tachycardia.

Hyperthyroidism:

Beta-blockade produced by SOTAHEXAL may mask certain clinical signs of hyperthyroidism (e.g. tachycardia). Patients suspected of developing thyrotoxicosis should be monitored carefully to avoid abrupt withdrawal of beta-blockade, which might be followed by an exacerbation of symptoms of hyperthyroidism, including thyroid storm.

Renal impairment:

Since sotalol, as contained in SOTAHEXAL, is mainly eliminated via the kidneys, the dose should be adjusted in patients with renal impairment (see section 4.3).

Psoriasis:

Beta-blocking medicines such as SOTAHEXAL have been reported rarely to exacerbate the symptoms of psoriasis vulgaris.

Life-threatening medicine interactions:

It is dangerous to administer SOTAHEXAL concomitantly with the following medicines: hypoglycaemic medicines, phenothiazines and various anti-dysrhythmic medicines. Such drug-drug interactions can have life-threatening consequences (see section 4.5).

Digoxin:

SPECIAL NOTE: Digitalisation of patients receiving long-term beta-blocker therapy such as SOTAHEXAL 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 (see section 4.5).

Phaeochromocytoma:

Patients with phaeochromocytoma usually require treatment with an alpha-adrenergic blocker (see section 4.4).

Myasthenia gravis:

SOTAHEXAL may unmask myasthenia gravis.

Lactose intolerance:

SOTAHEXAL contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take SOTAHEXAL.

4.5 Interaction with other medicines and other forms of interaction

Not recommended combinations:

Anti-dysrhythmics:

Class 1a anti-dysrhythmic medicines, such as disopyramide, quinidine, procainamide and flecainide and other anti-dysrhythmic medicines such as amiodarone and bepridil are not recommended as concomitant therapy with SOTAHEXAL, because of their potential to prolong refractoriness (see section 4.4). The concomitant use of other beta-blocking medicines with SOTAHEXAL may result in additive Class II effects.

Other medicines prolonging the QT-interval:

SOTAHEXAL should be given with extreme caution in conjunction with other medicines known to prolong the QT-interval such as phenothiazines, tricyclic antidepressants, terfenadine and astemizole. Other medicines that have been associated with an increased risk for torsade de pointes include erythromycin IV, halofantrine, pentamidine, and quinolone antibiotics.

Calcium channel blocking medicines:

Concurrent administration of beta-blocking medicines and calcium channel blockers has resulted in hypotension, bradycardia, conduction defects, and cardiac failure. Beta-blockers such as SOTAHEXAL should be avoided in combination with cardiodepressant calcium-channel blockers such as verapamil and diltiazem because of the additive effects on atrioventricular conduction, and ventricular function.

Potassium-depleting diuretics:

Hypokalaemia or hypomagnesaemia may occur, increasing the potential for torsade de pointes (see section 4.4).

Other potassium-depleting medicines:

Amphotericin B (IV route), corticosteroids (systemic administration), and some laxatives may also be associated with hypokalaemia. Potassium levels should be monitored and corrected appropriately during concomitant administration with SOTAHEXAL.

Clonidine:

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 beta-blockers are administered in these circumstances, the unopposed alpha receptor stimulation may potentiate this effect. Beta-blocking medicines may potentiate the rebound hypertension sometimes observed after discontinuation of clonidine; therefore, SOTAHEXAL should be discontinued slowly several days before the gradual withdrawal of clonidine.

Combinations that require precaution:

Digoxin glycosides:

Single and multiple doses of SOTAHEXAL do not significantly affect serum digoxin levels. Pro-dysrhythmic events were reported to be more common in sotalol treated patients also receiving digoxin glycosides; however, this may be related to the presence of CHF, a known risk factor for prodysrhythmia, in patients receiving digoxin glycosides. Association of digoxin glycosides with beta-blockers may increase auriculo-ventricular conduction time.

Catecholamine-depleting medicines:

Concomitant use of catecholamine-depleting medicines, such as reserpine, or alpha methyldopa, with SOTAHEXAL may produce an excessive reduction of resting sympathetic nervous tone. Patients should be closely monitored for evidence of hypotension and/or marked bradycardia which may produce syncope.

Insulin and oral hypoglycaemics:

Hyperglycaemia may occur and the dosage of anti-diabetic medicines may require adjustment. Symptoms of hypoglycaemia (tachycardia) may be masked by SOTAHEXAL.

Neuromuscular blocking medicines like tubocurarine:

The neuromuscular blockade is prolonged by beta-blocking medicines such as SOTAHEXAL.

Beta-2-receptor stimulants:

Beta-agonists may have to be administered in increased dosages when used concomitantly with SOTAHEXAL.

Medicine/laboratory interaction:

The presence of sotalol, as contained in SOTAHEXAL, in the urine may result in falsely elevated levels of urinary metanephrine when measured by photometric methods. Patients suspected of having phaeochromocytoma and who are treated with SOTAHEXAL should have their urine screened utilising the HPLC assay with solid phase extraction.

4.6 Fertility, pregnancy and lactation

Pregnancy:

Safety and efficacy of SOTAHEXAL has not been established in pregnant women. Sotalol hydrochloride has been shown to cross the placenta and is found in amniotic fluid. Beta-blockers including SOTAHEXAL, reduce placental perfusion, which may result in intrauterine foetal death, immature and premature deliveries. Administration of beta-blockers such as SOTAHEXAL to pregnant women shortly before delivery may result in the newborn infants being born hypotonic, collapsed and hypoglycaemic. In addition, adverse effects (especially bradycardia) may occur in the foetus and neonate. There is an increased risk of cardiac and pulmonary complications in the neonate in the postnatal period. The neonate should be monitored very carefully for 48 to 72 hours after delivery if it was not possible to interrupt maternal therapy with SOTAHEXAL 2 to 3 days before the birthdate.

Lactation:

Sotalol passes into breast milk. Breastfeeding is therefore not recommended during the administration of SOTAHEXAL.

4.7 Effects on ability to drive and use machines

There is no data available, but the occasional occurrence of side effects such as dizziness and fatigue should be taken into account.

4.8 Undesirable effects

The most frequent adverse effects arise from the beta-blockade properties of SOTAHEXAL. The most significant adverse effects, however, are those due to pro-dysrhythmia, including torsade de pointes (see section 4.4). The most common adverse events leading to discontinuation of SOTAHEXAL are fatigue, bradycardia (< 50 bpm), dyspnoea, pro-dysrhythmia, asthenia and dizziness.

Adverse reactions are more common in patients with renal decompensation.

Blood and the lymphatic system disorders:

Frequency unknown: Non-thrombocytopenic purpura, thrombocytopenia, agranulocytosis, transient eosinophilia.

Psychiatric disorders:

Frequent: Anxiety, sleep disturbances, mood changes, depression.

Frequency unknown: Hallucinations, confusion.

A variety of neuropsychiatric disorders, ranging from vague fatigue and nightmares to overt psychosis, have been observed.

Nervous system disorders:

Frequent: Dizziness, light-headedness, headache, paraesthesia, syncope, pre-syncope, taste abnormalities.

Frequency unknown: Peripheral neuropathy.

Eye disorders:

Frequent: Visual disturbances.

Less frequent: Reduced lacrimation.

Ear and labyrinth disorders:

Frequent: Hearing disturbances.

Cardiac disorders:

Frequent: Torsade de pointes, dysrhythmia, dyspnoea, chest pain, bradycardia, palpitations, ECG abnormalities, AV-conduction defect, pro-dysrhythmia, heart failure (see section 4.4).

Vascular disorders:

Frequent: Hypotension.

Frequency unknown: Raynaud's disease, aggravation of claudication intermittent, painful cold extremities.

Severe peripheral vascular disease and even peripheral gangrene may be precipitated.

Respiratory, thoracic and mediastinal disorders:

Less frequent: In patients with bronchial asthma or a history of asthmatic complaints, bronchitis and other pulmonary diseases, bronchospasm may occur.

Frequency unknown: Pneumonitis, pulmonary fibrosis and pleurisy.

Gastrointestinal disorders:

Frequent: Abdominal pain, nausea, vomiting, diarrhoea, dyspepsia, flatulence, dry mouth.

Frequency unknown: Constipation.

Skin and subcutaneous tissue disorders:

Frequency unknown: Rash, pruritus, alopecia, exacerbation of symptoms of psoriasis, hyperhidrosis.

Musculoskeletal and connective tissue disorders:

Frequent: Muscle cramps.

Frequency unknown: Myopathy, sclerosing peritonitis, retroperitoneal fibrosis.

Reproductive system and breast disorders:

Frequent: Sexual dysfunction.

General disorders and administration site conditions:

Frequent: Fatigue, asthenia, fever, oedema.

Investigations:

Frequency unknown: Formation of antinuclear antibodies has been reported.

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

Suspected adverse reactions can also be reported directly to the HCR via Patientsafety.sacg@novartis.com.

4.9 Overdose

Intentional or accidental overdose with sotalol, as contained in SOTAHEXAL, has resulted in death. Haemodialysis results in a large reduction of plasma levels of sotalol.

Symptoms and treatment:

The most common signs to be expected are bradycardia and hypotension, congestive heart failure, bronchospasm and hypoglycaemia.

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

In cases of massive intentional overdose (2 to 16 g) of sotalol, as contained in SOTAHEXAL, the following clinical findings were observed:

Hypotension, bradycardia, prolongation of QT-interval, premature ventricular complexes, ventricular tachycardia, torsade de pointes.

If an overdose occurs, therapy with SOTAHEXAL should be discontinued and the patient observed closely.

Gastric lavage should be performed within four hours of suspected overdose. Repeated activated charcoal is necessary in severe overdose. Artificial respiration may be necessary.

In addition, the following therapeutic measures are recommended:

Bradycardia: Atropine (0,5 to 2 mg IV; if the response is inadequate, glucagon may be given intravenously), another anti-cholinergic medicinal product, a beta-adrenergic agonist (isoprenaline, 5 micrograms per minute, up to 25 micrograms, by slow IV injection) or transvenous cardiac pacing.

Heart block (second and third degree): Transvenous cardiac pacing.

Hypotension: epinephrine (Adrenaline) rather than isoprenaline or norepinephrine (noradrenaline) may be useful, depending on associated factors.

Bronchospasm: Aminophylline (IV or inhaled) or beta-2-receptor stimulant (aerosol).

Torsade de pointes: Cardioversion, transvenous cardiac pacing, epinephrine (adrenaline) and/or magnesium sulphate.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 5.2 Medicines affecting autonomic functions – adrenolytics (sympatholytics)

Sotalol hydrochloride is a synthetic β-adrenergic blocking agent. It is non-cardio selective and is reported to lack both intrinsic sympathomimetic and membrane-stabilising properties. In addition to its class II anti-dysrhythmic activity, sotalol lengthens the duration of the action potential resulting in class III anti-dysrhythmic activity.

5.2 Pharmacokinetic properties

Sotalol is almost completely absorbed from the gastrointestinal tract and peak plasma concentrations occur 2 to 3 hours after a dose. The plasma elimination half-life is about 10 to 15 hours.

It is not metabolised and is excreted unchanged in the urine. It is not bound to plasma proteins, crosses the placenta and is found in breast milk, however, only small amounts are reported to cross the blood brain barrier and enter the CSF.

Sotalol is removed by dialysis.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal silicon dioxide

Hydroxypropylcellulose

Lactose monohydrate

Magnesium stearate

Maize starch

Sodium starch glycolate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

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

KEEP OUT OF THE REACH OF CHILDREN.

6.5 Nature and contents of container

SotaHexal 80: Securitainers containing 100 tablets.

SotaHexal 160: Securitainers containing 100 tablets.

6.6 Special precautions for disposal

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)

SOTAHEXAL 80: 29/5.2/0749

SOTAHEXAL 160: 29/5.2/0750

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

SotaHexal 80: 13 May 1997

SotaHexal 160: 12 March 1997

10 DATE OF REVISION OF THE TEXT

21 November 2020

Additional country registration details:

Country	*Product name*	*Scheduling status (or Category of distribution)*	*Registration number*
Namibia	Sotahexal 80	NS2	04/5.2/1355
	Sotahexal 160	NS2	04/5.2/1356

Name and address of manufacturer:

Salutas Pharma GmbH
Otto-von-Guericke-Allee 1
D-39179 Barleben
Germany

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