SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Sotalol 40 mg Tablets

Sotalol 80mg Tablets

Sotalol 160mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Sotalol Hydrochloride 40 mg

Sotalol Hydrochloride 80 mg

Sotalol Hydrochloride 160 mg

For excipients, see 6.1

3 PHARMACEUTICAL FORM

Tablets;
Round white to off white flat bevelled edge tablets.

Round white to off white flat bevelled edged tablets with a score line on one side.

The score line is not intended for breaking the tablet.

Round blue flat bevelled edge tablets with a score line on one side.

The score line is not intended for breaking the tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Ventricular arrhythmias:

- Treatment of life-threatening ventricular tachyarrhythmias.
- Treatment of symptomatic non-sustained ventricular tachyarrhythmias.

Supraventricular arrhythmias:

- Prophylaxis of paroxysmal atrial tachycardia, paroxysmal atrial fibrillation, paroxysmal A-V nodal re-entrant tachycardia, paroxysmal A-V re-entrant tachycardia using accessory pathways, and paroxysmal supraventricular tachycardia after cardiac surgery
- Maintenance of normal sinus rhythm following conversion of atrial fibrillation or atrial flutter.

4.2 Posology and method of administration

Posology

Paediatric population
There is no relevant use of Sotalol in the paediatric population.
The initiation of treatment or changes in dosage with Sotalol should follow an appropriate medical evaluation including ECG control with measurement of the corrected QT interval, and assessment of renal function, electrolyte balance, and concomitant medications (see section 4.4).

As with other antiarrhythmic agents, it is recommended that Sotalol be initiated and doses increased in a facility capable of monitoring and assessing cardiac rhythm. The dosage must be individualized and based on the patient's response. Proarrhythmic events can occur not only at initiation of therapy, but also with each upward dosage adjustment.

In view of its beta-adrenergic blocking properties, treatment with Sotalol should not be discontinued suddenly, especially in patients with ischaemic heart disease (angina pectoris, prior acute myocardial infarction) or hypertension, to prevent exacerbation of the disease (see section 4.4).

Method of Administration
The following dosing schedule can be recommended:

The initial dose is 80 mg, administered either singly or as two divided doses.

Oral dosage of Sotalol should be adjusted gradually allowing 2-3 days between dosing increments in order to attain steady-state, and to allow monitoring of QT intervals. Most patients respond to a daily dose of 160 to 320 mg administered in two divided doses at approximately 12 hour intervals. Some patients with life-threatening refractory ventricular arrhythmias may require doses as high as 480-640 mg/day. These doses should be used under specialist supervision and should only be prescribed when the potential benefit outweighs the increased risk of adverse events, particularly proarrhythmias (see section 4.4).

Children*:* Sotalol Tablets are not intended for administration to children.

Dosage in renally impaired patients*:* Because Sotalol is excreted mainly in urine, the dosage should be reduced when the creatinine clearance is less than 60 ml/min according to the following table:

Creatinine clearance (ml/min)	Adjusted doses
> 60	Recommended Sotalol Dose
30-60	½ recommended Sotalol Dose
10-30	¼ recommended Sotalol Dose
< 10	Avoid

The creatinine clearance can be estimated from serum creatinine by the Cockroft and Gault formula:

Men:
((140-age) × weight (kg)) / (72×serum creatinine (mg/dl))

Women: idem×0.85

When serum creatinine is given in µmol/l, divide the value by 88.4 (1 mg/dl = 88.4 µmol/l).

Dosage in hepatically impaired patients: Since Sotalol is not subject to first-pass metabolism, patients with hepatic impairment show no alteration in clearance of Sotalol. No dosage adjustment is required in hepatically impaired patients.

4.3 Contraindications

- Sotalol should not be used where there is evidence of sick sinus syndrome;
- second and third-degree AV heart block unless a functioning pacemaker is present;
- congenital or acquired long QT syndromes;
- QTc longer than 450 milliseconds (500 milliseconds in patients with ventricular conduction disorders
- torsades de pointes;
- symptomatic sinus bradycardia;
- uncontrolled congestive heart failure;
- cardiogenic shock;
- anaesthesia that produces myocardial depression;
- untreated phaeochromocytoma;
- hypotension (except due to arrhythmia);
- Raynaud's phenomenon and severe peripheral circulatory disturbances;
- history of chronic obstructive airway disease or bronchial asthma (a warning will appear on the label);
- hypersensitivity to the active substance or to any of the excipients listed in section 6.1 ;
- metabolic acidosis;
- renal failure (creatinine clearance < 10ml/min)
- hypokalaemia and hypomagnesemia

4.4 Special warnings and precautions for use

Abrupt withdrawal: Hypersensitivity to catecholamines is observed in patients withdrawn from beta-blocker therapy. Occasional cases of exacerbation of angina pectoris, arrhythmias, and in some cases, myocardial infarction have been reported after abrupt discontinuation of beta-blocker therapy. Patients should be carefully monitored when discontinuing chronically administered

Sotalol, particularly those with ischaemic heart disease. If possible the dosage should be gradually reduced over a period of one to two weeks. Because coronary artery disease is common and may be unrecognised in patients receiving Sotalol, abrupt discontinuation in patients with arrhythmias may unmask latent coronary insufficiency. In addition, hypertension may develop.

Proarrhythmia: The most dangerous adverse effect of Class I and Class III antiarrhythmic drugs (such as sotalol) is the aggravation of pre-existing arrhythmias or the provocation of new arrhythmias. Drugs that prolong the QT-interval may cause torsades de pointes, a polymorphic ventricular tachycardia associated with prolongation of the QT-interval. Experience to date indicates that the risk of torsades de pointes is associated with the prolongation of the QT-interval, reduction of the heart rate, reduction in serum potassium and magnesium levels, high plasma sotalol concentrations and with the concomitant use of sotalol and other medications which have been associated with torsades de pointes (see section 4.5). Females may be at increased risk of developing torsades de pointes. ECG monitoring immediately prior to or following the episodes usually reveals a significantly prolonged QT interval and a significantly prolonged QTc interval. In clinical trials, Sotacor generally has not been initiated to patients whose pretreatment QTc interval exceeded 450 msec. Sotacor should be titrated very cautiously in patients with prolonged QT intervals.

The incidence of torsades de pointes is dose dependent. Torsades de pointes usually occurs within7 days of initiating therapy or escalation of the dose and can progress to ventricular fibrillation. Most torsade de pointes resolve spontaneously but may be associated with symptoms (e.g. syncope).

In clinical studies in patients with PDA/ventricular fibrillation, the incidence of severe proarrhythmias (torsade de pointes or new PDA) was <2 at doses up to 320mg. The incidence more than doubled at higher doses.

Clinical studies for arrhythmia: During clinical trials, 4.3% of 3257 patients with arrhythmias experienced a new or worsened ventricular arrhythmia, including sustained ventricular tachycardia (approximately 1%) and torsade de pointes (2.4%). In addition, in approximately 1% of patients, deaths were considered possibly drug related. In patients with other, less serious, ventricular arrhythmias and supraventricular arrhythmias, the incidence of torsade de pointes was 1% and 1.4%, respectively.

Serious proarrhythmias including torsade de pointes were dose related as indicated below:

Percent Incidence of Serious Proarrhythmias * by Dose For Patients With Sustained VT/VF		
Daily Dose (mg)	**Incidence of Serious Proarrhythmias***	**Patients (n)**
1-80	0	(0/72)

81-160	0.5%	(4/838)
161-320	1.8%	(17/960)
321-480	4.5%	(21/471)
481-640	4.6%	(15/327)
>640	6.8%	(7/103)

*Torsade de Pointes or New Sustained VT/VF

In clinical trials of patients with sustained VT/VF the incidence of severe proarrhythmia (torsades 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 torsades de pointes were excessive prolongation of the QT_C 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 proarrhythmia (7%).

Proarrhythmia can occur not only at the start of treatment, but also at each dose increase; This usually occurs within 7 days of starting treatment or at dose escalation. By giving an initial dose of 80 mg sotalol daily, which is then gradually increased, the risk of proarrhythmia is reduced. If the QTC is longer than 450 milliseconds (500 milliseconds in patients with ventricular conduction disorders), special caution should be exercised and discontinuation should be considered if the QTC is prolonged to more than 500 milliseconds during treatment (550 milliseconds in patients with ventricular conduction disorders). As many factors can play a role in the onset of torsade de pointes, caution should always be exercised regardless of the QTC interval.
Electrolyte disturbances: Sotalol 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 torsades 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 drugs.

Congestive heart failure: Beta-blockade 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, digitalis, etc); a low initial dose and careful dose titration is appropriate.

Recent MI: In post-infarction patients with impaired left ventricular function, the risk versus benefit of sotalol administration must be considered. Careful monitoring and dose titration are critical during initiation and follow-up of therapy. The adverse results of clinical trials involving antiarrhythmic drugs (i.e. apparent increase in mortality) suggest that Sotalol should be avoided in patients with left ventricular ejection fractions ≤ 40% without serious ventricular arrhythmias. In a large controlled trial in patients with a recent

myocardial infarction without heart failure, who did not necessarily have ventricular arrhythmias, oral sotalol HCl treatment was associated with a non-statistically significant risk reduction in mortality compared to the placebo group (18%). In this post-infarction study using a fixed dose of 320 mg once daily and in a second small randomized trial in high-risk post-infarction patients with left ventricular ejection fractions ≤40% treated with high doses (640 mg/day), there were suggestions of an excess of early sudden deaths.

Electrocardiographic Changes: Excessive prolongation of the QT-interval, > 500 msec, can be a sign of toxicity and should be avoided (see Proarrhythmias above). Sinus bradycardia has been observed very commonly in arrhythmia patients receiving sotalol in clinical trials. Bradycardia increases the risk of torsades 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%.

Prinzmetal Angina: Drugs with beta-adrenoreceptor blocking properties, such as sotalol, should be used with caution in patients suffering from Prinzmetal angina due to increased risk of angina pectoris.
Anaphylactic reactions: 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 patients may be unresponsive to the usual doses of adrenaline used to treat the allergic reaction.

Anaesthesia: As with other beta-blocking agents, Sotalol should be used with caution in patients undergoing surgery and in association with anaesthetics that cause myocardial depression, such as cyclopropane or trichloroethylene.

Diabetes mellitus: Sotalol 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.

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

Renal impairment: As sotalol is mainly eliminated via the kidneys the dose should be adjusted in patients with renal impairment (see section 4.2).

Psoriasis: Beta-blocking drugs have been reported rarely to exacerbate the symptoms of psoriasis vulgaris.

Impact on laboratory values:
The presence of sotalol in urine may result in falsely elevated values of methanephrine in photometric measurement methods. The urine of patients with suspected pheochromocytoma treated with sotalol should be monitored by HPLC method.

Important information regarding the ingredients of this medicine

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

4.5 Interactions with Other Medicaments and Other Forms of Interaction

Antiarrhythmics: Class Ia antiarrhythmic drugs, such as disopyramide, quinidine and procainamide, Class Ic antiarrhythmics such as propafenone and flecainide, Class III antiarrhythmics such as amiodarone, ibutilide, and dofetilide, and other antiarrhythmics such as bepridil are not recommended as concomitant therapy with Sotalol, because of their potential to prolong refractoriness (see section 4.4). The concomitant use of other beta-blocking agents with Sotalol may result in additive Class II effects.

Other drugs prolonging the QT-interval: Sotalol should be given with extreme caution in conjunction with other drugs known to prolong the QT-interval (Note: the following list is not exhaustive, the product information for medicines taken at the same time should always be read):

- Antiarrhythmics: class Ia (quinidine, disopyramide, procainamide, ajmaline), Ic (flecainide, cibenzolinide), III (amiodarone, azimilide, dofetilide, dronedarone, ibutilide);
- Antipsychotics, phenothiazines (mesoridazine, thioridazine, levomepromazine, chlorpromazine), butyrofenone (haloperidol, droperidol, fluvoxamine), others (pimozide, sultopride, amisulpride, sertindole);
- antidepressants: SSRI (citalopram, escitalopram, fluoxetine, paroxetine, sertraline, fluvoxamine), tricyclic antidepressants (Clomipramine, amitriptyline, desipramine, imipramine, nortriptyline);
- antibiotics: fluoroquinolones (ciprofloxacin, moxifloxacin, gatifoxacin, levofloxacin), macrolide (azithromycin, clarithromycin, erythromycin, roxithromycin)
- antimalarial drugs: halofantrine, chloroquine, artenimol;
- antihistamines: famotidine, terfenadine, promethazine, diphenhydramine;
- prokinetics/antiemetics: cisapride, domperidone, ondansetron;
- protein kinase inhibitors: vemurafenib, sunitinib, sorafenib;
- Other: arsenic trioxide, donepezil, propofol, trazodone, hydrocodone, methadone, bepridil, ranolazine, hydroxyzine, fluconazole, papaverine, anagrelide, pentamidine).
- mizolastine, levacetylmethadol and astemizole.

Other drugs that have been associated with an increased risk for torsades de pointes include erythromycin IV, halofantrine, pentamidine and quinolone antibiotics.

Floctafenine: beta-adrenergic blocking agents may impede the compensatory cardiovascular reactions associated with hypotension or shock that may be induced by Floctafenine.

Calcium channel blocking drugs: Concurrent administration of beta-blocking agents and calcium channel blockers has resulted in hypotension, bradycardia, conduction defects, and cardiac failure. Beta-blockers 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. Severe hypotension and heart failure occasionally can occur with nifedipine and possibly with other dihydropyridines.

Potassium-depleting diuretics: Hypokalaemia or hypomagnesaemia may occur, increasing the potential for torsade de pointes (see section 4.4).

Other potassium-depleting drugs: 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 Sotalol.

Proton pump inhibitors: Hypomagnesemia may occur that increases the potential for torsades de pointes (omeprazole, lansoprazole, pantoprazole, esomeprazole) (see section 4.4).

Clonidine: Beta-blocking drugs may potentiate the rebound hypertension sometimes observed after discontinuation of clonidine; therefore, the beta-blocker should be discontinued slowly several days before the gradual withdrawal of clonidine.

The following combinations with sotalol may require dose adjustment

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

Catecholamine-depleting agents: Concomitant use of catecholamine-depleting drugs, such as reserpine, guanethidine, or alpha methyldopa, with a beta-blocker 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 antidiabetic drugs may require adjustment. Symptoms of hypoglycaemia (tachycardia) may be masked by beta-blocking agents.

Neuromuscular blocking agents like Tubocurarin: The neuromuscular blockade is prolonged by beta-blocking agents.

Beta-2-receptor stimulants: Patients in need of beta-agonists should not normally receive Sotalol. However, if concomitant therapy is necessary beta-agonists may have to be administered in increased dosages.

Epinephrine: Pronounced hypertension and bradycardia have been reported in patients treated with non-selective beta-receptor blocking agents (e.g. propranolol) and epinephrine.

Phenylpropanolamine: Beta receptor blockers can trigger paradoxical hypertensive reactions in patients taking large doses of phenylpropanolamine.

Use with Mefloquine can lead to an increased risk of bradycardia.

Ergotamine: concomitant use of ergotamine can increase peripheral vasoconstriction.

Sympathomimetics: severe hypertension with adrenaline and noradrenaline and possibly with dobutamine.

Theophylline: sotalol should be avoided on pharmacological grounds (bronchospasm).

Tropisetron: caution is advised if the patient is taking tropisetron as there is a risk of ventricular arrhythmias.

Drugs causing enhanced hypotensive effects of sotalol: aldesleukin, alprostadil, anxiolitics and hypnotics.

Drugs which antagonise the hypotenitve effects of sotalol:
NSAID's, oestrogens and combined oral contraceptives, carbenoxolone and xamoterol.

Drug/laboratory interaction: The presence of sotalol 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 Sotalol should have their urine screened utilizing the HPLC assay with solid phase extraction.

4.6 Fertility, Pregnancy and lactation

Pregnancy: Animal studies with sotalol hydrochloride have shown no evidence of teratogenicity or other harmful effects on the foetus. Although there are no adequate and well-controlled studies in pregnant women, sotalol hydrochloride has been shown to cross the placenta and is found in amniotic fluid. Beta-blockers reduce placental perfusion, which may result in

intrauterine foetal death, immature and premature deliveries. In addition, adverse effects (especially hypoglycaemia, hypotension and bradycardia) may occur in foetus and neonate. There is an increased risk of cardiac and pulmonary complications in the neonate in the postnatal period. Therefore, Sotalol should be used in pregnancy only if the potential benefits outweigh the possible risk to the foetus. The neonate should be monitored very carefully for 48-72 hours after delivery if it was not possible to interrupt maternal therapy with Sotalol 2-3 days before the birthdate.

Breast feeding: Most beta-blockers, particularly lipophilic compounds, will pass into breast milk although to a variable extent. Breast feeding is therefore not recommended during administration of these compounds.

4.7 Effects on ability to drive and use machines

There are no data available, but the occasional occurrence of side-effects such as dizziness and fatigue should be taken into account (see section 4.8 Undesirable effects).

4.8 Undesirable effects

Sotalol is well tolerated in the majority of patients, with the most frequent adverse effects arising from its beta-blockade properties. Adverse effects are usually transient in nature and rarely necessitate interruption of, or withdrawal from treatment. These include dyspnoea, fatigue, dizziness, headache, fever, excessive bradycardia and/or hypotension. If they do occur, they usually disappear when the dosage is reduced. The most significant adverse effects, however, are those due to proarrhythmia, especially in patients treated for ventricular arrhythmias including torsades de pointes, persistent ventricular tachycardia and ventricular fibrillation (see section 4.4).

Frequency is defined using the following convention: Very common (≥ 1/10); common (≥ 1/100, < 1/10); uncommon (≥ 1/1,000, < 1/100); rare (≥ 1/10,000, < 1/1,000); very rare (< 1/10,000) and Not known frequency (cannot be calculated from the available data) including isolated reports.

The following are adverse events considered related to therapy with Sotalol.

System Organ Class	**Very common**	**Common**	**Not Known**
Blood and Lymphatic system disorders		Hypotension	Thrombocytopenia

Cardiac Disorders	Bradycardia Palpitations Electrocardiogram abnormal	Hypotension Arrhythmia Syncope Presyncope Cardiac Failure	Impaired peripheral circulation Atrioventricular block Peripheral vascular disease (Raynaud's syndrome, claudication intermittent) Angina pectoris
Skin and subcutaneous tissue disorders	Exanthema	Rash	Alopecia Hyperhidrosis Psoriasis-like conditions
Respiratory, thoracic and mediastinal disorders	Dyspnoea		Bronchospasm
Gastrointestinal Disorders	Diarrhoea Vomiting	Nausea Dyspepsia Abdominal pain Flatulence	
Musculoskeletal, Connective Tissue and bone Disorders		Muscle Spasms	
Nervous System Disorders	Headache Dizziness	Fatigue Asthenia Light-headedness Paraesthesia Dysgeusia	
Psychiatric Disorders	Sleep disorder	Mood swings Depression Anxiety	
Reproductive system and Breast Disorders		Sexual dysfunction	
Eye Disorders		Visual disturbance	
Ear and Labyrinth		Hearing disturbances	

Disorders			
General Disorders and Administration site conditions	Asthenia Chest pain Edema	Pyrexia Fatigue	

In clinical trials, 3256 patients with cardiac arrhythmias (1363 with sustained ventricular tachycardia) received oral Sotacor, of whom 2451 received the drug for at least two weeks. The most significant adverse events were torsade de pointes and other serious new ventricular arrhythmias (see section 4.4), which occurred at the following rates:

Patient Populations			
	VT/VF (n=1,363)	**NSVT/PVC** (n=946)	**SVA** (n=947)
Torsade de Pointes	4.1%	1.0%	1.4%
Sustained VT/VF	1.2%	0.7%	0.3%

VT = ventricular tachycardia; VF = ventricular fibrillation; NSVT = non sustained ventricular tachycardia; PVC = premature ventricular contraction; SVA = supraventricular arrhythmia.

Increased levels of antinuclear antibodies (ANA) have been observed, but the clinical relevance of this is unclear.

Overall, discontinuation because of unacceptable adverse events was necessary in 18% of all patients in cardiac arrhythmia trials. The most common adverse events leading to discontinuation of Sotacor are listed in the table below:

- fatigue	4%
- bradycardia (<50 bpm)	3%
- dyspnoea	3%
- proarrythmia	2%
- asthenia	2%
- dizziness	2%

Cold and cyanotic extremities, Raynauds's phenomenon, increase in existing intermittent claudication and dry eyes have been seen in association with other beta-blockers.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme Website:

www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Intentional or accidental overdosage with Sotalol has rarely resulted in death. Haemodialysis results in a large reduction of plasma levels of sotalol.

Symptoms and treatment of overdosage: The most common signs to be expected are bradycardia, congestive heart failure, hypotension, bronchospasm, hypoglycaemia and seizures (including hypoglycaemic seizures). In cases of massive intentional overdosage (2-16 g) of Sotalol the following clinical findings were seen: hypotension, bradycardia, QT prolongation, premature gastric complexes, ventricular tachycardia and *torsades de pointes*. Overdoses with sotalol can cause serious arrhythmias. Risk of CNS depression and seizures in more severe cases.

If overdosage occurs, therapy with Sotalol should be discontinued and the patient observed closely. In addition, if required, the following therapeutic measures are suggested:

Bradycardia: Atropine (0.5 to 2mg IV), another anticholinergic drug, a beta-agonist (isoprenaline, 5 microgram per minute, up to 25 microgram, by slow IV injection) or transvenous pacemaker.

Heart Block (second and third degree): Transvenous pacemaker.

Hypotension: Adrenaline rather than isoprenaline or noradrenaline may be useful, depending on associated factors. Under monitoring of homodynamics, supply fluid i.v. to adequate fill pressure. If necessary, dobutamine and possibly the addition of norepinephrine.

Bronchospasm: Aminophylline or aerosol beta-2-receptor stimulant.

Torsades de pointes: DC cardioversion, pacemaker, and on vital indication, adrenaline, Isoprenaline infusion, and/or magnesium sulphate.

Other ventricular extrabeats/dysrhythmias: Lidocaine can be tried.
Other symptomatic treatment may be necessary, e.g. in case of respiratory effects, seizures and metabolic disorders.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Beta Blocking agents, non selective
ATC code: C07A A07

D, L-sotalol is a non-selective hydrophilic beta-adrenergic receptor blocking agent, devoid of intrinsic sympathomimetic activity or membrane stabilizing activity.

Sotalol has both beta-adrenoreceptor blocking (Vaughan Williams Class II) and cardiac action potential duration prolongation (Vaughan Williams Class III) antiarrhythmic properties. Sotalol has no known effect on the upstroke velocity and therefore no effect on the depolarisation phase.

Sotalol uniformly prolongs the action potential duration in cardiac tissues by delaying the repolarisation phase. Its major effects are prolongation of the atrial, ventricular and accessory pathway effective refractory periods.

The Class II and III properties may be reflected on the surface electrocardiogram by a lengthening of the PR, QT and QTC (QT corrected for heart rate) intervals with no significant alteration in the QRS duration.

The d- and l-isomers of sotalol have similar Class III antiarrhythmic effects while the l-isomer is responsible for virtually all of the beta-blocking activity. Although significant beta-blockade may occur at oral doses as low as 25 mg, Class III effects are usually seen at daily doses of greater than 160 mg.

Its beta-adrenergic blocking activity causes a reduction in heart rate (negative chronotropic effect) and a limited reduction in the force of contraction (negative inotropic effect). These cardiac changes reduce myocardial oxygen consumption and cardiac work. Like other beta-blockers, sotalol inhibits renin release. The renin-suppressive effect of sotalol is significant both at rest and during exercise. Like other beta adrenergic blocking agents, Sotalol produces a gradual but significant reduction in both systolic and diastolic blood pressures in hypertensive patients. Twenty-four-hour control of blood pressure is maintained both in the supine and upright positions with a single daily dose.

5.2 Pharmacokinetic properties

Absorption
The absorption is reduced by approximately 20% when administered with a standard meal, in comparison to fasting conditions.

Distribution
Over the dosage range 40-640 mg/day Sotalol displays dose proportionality with respect to plasma levels. Distribution occurs to a central (plasma) and a peripheral compartment, with an elimination half-life of 10-20 hours. The bioavailability of oral sotalol is essentially complete (greater than 90%). After oral administration, peak levels are reached in 2.5 to 4 hours, and steady-state plasma levels are attained within 2-3 days.

Metabolism

Sotalol does not bind to plasma proteins and is not metabolised. There is very little inter-subject variability in plasma levels. Sotalol crosses the blood brain barrier poorly, with cerebrospinal fluid concentrations only 10% of those in plasma.

Elimination
The primary route of elimination is renal excretion. Approximately 80 to 90% of a dose is excreted unchanged in the urine, while the remainder is excreted in the faeces.
Lower doses are necessary in conditions of renal impairment (see section 4.2).
Age does not significantly alter the pharmacokinetics, although impaired renal function in geriatric patients can decrease the excretion rate, resulting in increased drug accumulation.

5.3 Preclinical safety data
There are no pre-clinical data of relevance to the prescriber additional to those stated in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Calcium Hydrogen Phosphate Dihydrate
Maize Starch
Povidone K30
Sodium Starch Glycolate, Type A
Talc
Magnesium Stearate

6.2 Incompatibilities
None known.

6.3 Shelf life
36 months

6.4 Special precautions for storage
Store below 25°C.

6.5 Nature and contents of container
PVC/PVdC - aluminium foil blister pack containing 28, 30, 50 or 56 tablets.

6.6 Special precautions for disposal
None stated.

7 MARKETING AUTHORISATION HOLDER

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United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 17907/0258
PL 17907/0259
PL 17907/0260

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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14/05/2025