SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Sotalol 80 mg Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 80 mg sotalol hydrochloride.

Excipient with known effect:
Lactose

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet

80 mg: Light blue, oval-shaped tablet, scored on one side and debossed with the number "93" and "61" on each side of the score, plain on the other side.

The tablet can be divided into equal doses.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Sotalol is indicated in adults for prophylaxis of:
- life-threatening ventricular tachycardias;
- documented symptomatic and disabling ventricular tachycardias in the absence of uncontrolled heart failure;
- documented supraventricular tachycardias in the absence of uncontrolled heart failure when the need for treatment is established. (e.g. maintenance of sinus rhythm after conversion of atrial fibrillation or atrial flutter.)

4.2. Posology and method of administration

Posology
The initiation of treatment or change in dosage should follow an appropriate medical evaluation, including ECG control with measurement of the corrected QT interval and potassium levels, assessment of renal function and taking into account concomitant medication (see section 4.5).

As with other antiarrhythmic substances, it is recommended that Sotalol is initiated and doses increased under ECG control, because proarrhythmic events can occur not only at the initiation of therapy but also with every upward dosage adjustment.

The treatment of life-threatening ventricular tachycardias must be initiated under monitoring in a hospital environment.

The initial dose is 80 mg administered either as a single or as two divided doses administered at 12 hours interval. Dosing increments should be separated by an interval of 2 or 3 days in order to attain a steady state and allow monitoring of QT intervals.
Most patients respond to a daily dose of 160 to 320 mg in two (e.g. 2x 160 mg) or three (e.g. 3x 80 mg) divided doses per day.

Some patients who have life-threatening arrhythmias may require doses as high as 480 mg or 640 mg/day; however, these doses should be used under specialist supervision and only be prescribed when the potential benefit outweighs the increased risk of adverse events, in particular proarrhythmia.

Renal impairment
The dosage should be adjusted according to the creatinine clearance, because sotalol is excreted mainly in urine. The heart rate (should not fall below 50 beats per minute) and the clinical effect should also be considered.

Creatinine Clearance (ml/min)	Recommended posology
> 60	Usual dose
30 - 60	Half-dose
10 - 30	Quarter dose
< 10	Avoid sotalol

Cockcroft & Gault formula:

Men:
$$\frac{(140 - \text{age}) \times \text{weight (kg)}}{72 \times \text{serum creatinine (mg/dl)}}$$

Women: idem x 0.85.

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

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

Elderly
Age in itself is not a reason to adapt the initial dosage. Reduction in renal function due to old age may necessitate dose adaptation (see also 'Renal impairment').

Paediatric population
Due to lack of data, sotalol is not intended for use in children.

Method of administration
The tablets should be taken with a sufficient amount of liquid (e.g. a glass of water) and swallowed whole.

4.3. Contraindications

Sotalol is contraindicated in the following situations:
- hypersensitivity to the active substance, sulfonamides or to any of the excipients listed in section 6.1
- long QT syndromes (congenital or acquired)
- torsades de pointes
- bronchial asthma and chronic obstructive airway disease
- uncontrolled heart failure
- cardiogenic shock
- 2nd and 3rd degree atrioventricular heart block, unless a functioning pacemaker is present
- Prinzmetal angina pectoris

- sick sinus syndrome (including sino-atrial heart block) unless a functioning pacemaker is present
- bradycardia (< 50 beats/minute)
- Raynaud's phenomenon and peripheral circulatory disturbances
- untreated phaeochromocytoma
- arterial hypotension (except when due to arrhythmia)
- anaesthesia that produces myocardial depression
- severe renal failure (creatinine clearance < 10 ml/min)
- metabolic acidosis
- combination with substances that cause torsades de pointes:
  - class Ia antiarrhythmic agents (quinidine, hydroquinidine, disopyramide…),
  - other class III antiarrhythmic agents (amiodarone, dofetilide, ibutilide…),
  - some neuroleptics (thioridazine, chlorpromazine, levomepromazine, trifluoperazine, cyamemazine, sulpiride, sultopride, amisulpride, tiapride, pimozide, haloperidol, droperidol…),
  - other active substances e.g. bepridil, cisapride, diphenamil, erythromycin IV, mizolastine, vincamine IV, moxifloxacin…
- floctafenine (see section 4.5).

4.4. Special warnings and precautions for use

Warnings

Never withdraw the treatment abruptly in patients with angina pectoris: this could cause severe arrhythmias, myocardial infarction and sudden death. Because coronary artery disease is common and maybe unrecognised in patients receiving Sotalol, abrupt discontinuation in patients with arrhythmias may unmask latent coronary insufficiency. In addition, hypertension may develop.
It is recommended to monitor patients, especially those suffering from ischaemic heart disease, and to decrease the dose gradually over 1-2 weeks.

The most dangerous undesirable effect of antiarrhythmic active substances is the aggravation of pre-existing arrhythmias or the provocation of new arrhythmias. Active substances that prolong the QT interval, including sotalol, may cause torsades de pointes.

Factors favouring this effect have been identified:
- spontaneously long QT interval (> 450 ms) before treatment
- bradycardia (< 60 beats per minute)
- hypokalaemia or hypomagnesaemia (notably with concomitant treatment with proximal diuretics)
- high serum levels of sotalol, either by overdose, or by accumulation in renally impaired patients
- combination with other products favouring torsades de pointes (see section 4.3 and section 4.5)
- severe ventricular arrhythmias
- females may be at an increased risk of developing torsades de pointes.

The incidence of torsades de pointes is dose-dependent. Proarrhythmic events occur more often within the first week of treatment initiation or dose escalation. However, they may occur after a longer period of treatment even without any dose change. They may be symptomatic (syncopes), they may discontinue spontaneously or more rarely progress to ventricular fibrillation.
In clinical trials of patients with ventricular arrhythmias carrying a life-threatening risk (sustained ventricular tachycardias or ventricular fibrillation), the incidence of severe

proarrhythmias (torsades de pointes or new ventricular tachycardias or ventricular fibrillation) was less than 2 % at doses up to 320 mg. The incidence is more than doubled for higher doses.

The highest risk of developing severe proarrhythmic events with sotalol (7%) occurs in patients with sustained ventricular tachycardia and heart failure. The risk of proarrhythmic events may be reduced by initiating therapy with 80 mg, with gradual upward dose titration thereafter.

During therapy, medical monitoring and ECG controls should be performed at regular intervals. If the ECG parameters deteriorate (e.g. 25% or greater prolongation of the QRS or QT interval, 50% or greater prolongation of the PQ interval or if the QTc interval exceeds 480 ms) or if the frequency and severity of arrhythmias increase, a re-evaluation of the benefit/risk ratio should be considered.

Precautions for use

- *Bradycardia*
  If heart rate drops to below 50-55 beats per minute at rest and the patient shows symptoms associated with bradycardia, the posology must be reduced. Bradycardia increases the risk of torsades de pointes.
- *First degree atrioventricular heart block*
  Given its negative dromotropic effect, sotalol should be administered with caution to patients with first degree atrioventricular heart block.
- *Heart failure*
  Caution is advised when initiating sotalol therapy or during adjustment of dose, in patients with left ventricular dysfunction controlled by therapy (such as angiotensin converting enzyme inhibitors, diuretics, digitalis...).
  Due to its beta-blockade properties, sotalol can further depress myocardial contractility and precipitate sudden decompensation of severe cardiac failure.
- *Recent myocardial infarction*
  The benefit/risk ratio of sotalol administration should be evaluated in post-infarction patients, with impaired left ventricular function. If this treatment is deemed necessary, its initiation and any subsequent changes in posology must be carefully monitored. The adverse results of clinical trials involving antiarrhythmic drugs (i.e. apparent increase in mortality) suggests that Sotalol should be avoided in patients with left ventricular ejection fraction ≤40% without serious ventricular arrhythmia.
- *Electrolytic disturbances*
  Sotalol should not be used in patients with hypokalaemia or hypomagnesaemia prior to correction of the imbalance; these conditions can exaggerate the degree of QT prolongation, and increase the potential for torsades de pointes. The electrolytic and acid-base balance must be closely monitored in patients with severe or prolonged diarrhoea or patients receiving concomitant magnesium- and/or potassium-depleting medicinal products.
- *Anaphylaxis*
  Due to its beta-blockade properties, sotalol may aggravate anaphylactic reactions and cause resistance to treatment by the usual doses of adrenaline in patients prone to severe anaphylactic reactions, whatever their origin, and especially if they are due to floctafenine (see section 4.5) or iodised contrast media or occur during desensitisation therapy.
- *Thyrotoxicosis*
  Due to its beta-blockade properties, sotalol can mask the certain clinical signs of hyperthyroidism (e.g., tachycardia) as well as cardiovascular signs of thyrotoxicosis. 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.
- *Psoriasis*
  As exacerbation of this illness has been reported with beta-blockers, the indication needs to be weighed up.

- *Elderly*
  The contraindications must imperatively be respected. Effort should be made to initiate treatment with a low dose and to ensure strict follow-up.
- *Renal impairment*
  In patients with renal impairment, the dose should be adjusted according to renal function (see section 4.2).
- *Diabetes mellitus*
  Inform the patient and reinforce glycaemic self-monitoring at the initiation of treatment. The precursor signs of hypoglycaemia may be masked, in particular tachycardia, palpitations and sweating.
- *Electrocardiographic changes*
  Strict monitoring and re-evaluation of the benefit/risk ratio are required if excessive QTc-interval prolongation (> 480 ms) is observed. The excessive prolongation of the QT interval, >500 ms, can be sign of toxicity and should be avoided. The risk of torsades de pointes is proportional to the degree of QT interval prolongation. 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%.
- *General anaesthesia*
  Due to its beta-blockade properties, sotalol can decrease reflex tachycardia and increase the risk of hypotension. Continuation of treatment with sotalol reduces the risk of arrhythmia, myocardial ischaemia and hypertension crises. The anaesthetist should be informed that the patient is being treated with sotalol.
  If it is judged necessary to discontinue the treatment, a 48 hour withdrawal is considered sufficient to allow sensitivity to catecholamines to re-develop. In certain cases, treatment with sotalol cannot be interrupted.
  In patients suffering from ischaemic heart disease or coronary heart disease, it is preferable to continue the treatment up to the intervention, given the risk associated with abrupt discontinuation of beta-blockers.
  In urgent cases or if it is impossible to stop the treatment, the patient should be protected from vagal predominance by sufficient atropine pre-medication, renewed according to requirements.
  The anaesthetics used should have minimal myocardial depressive action, and any blood loss should be compensated for.
- Sotalol IS GENERALLY NOT RECOMMENDED in combination with halofantrine, pentamidine, fluoroquinolones or methadone (see section 4.5), and during lactation.
- Sotalol is generally not recommended in association with certain medicinal products (see section 4.5, "Combinations not recommended").
- It is also not recommended with drugs which can induce hypertension (e.g. MAOIs).

Lactose
Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

The special properties of sotalol may cause serious arrhythmias (torsades de pointes), particularly in the presence of hypokalaemia and/or bradycardia. In terms of interactions with other medicinal products, it should be considered as an antiarrhythmic agent. Combination with other such agents is therefore VERY DELICATE, if not CONTRAINDICATED, and requires close clinical and ECG monitoring.

Contraindicated combinations

- **Floctafenine:** in case of floctafenine-induced shock or hypotension, sotalol impedes the compensatory cardiovascular reactions.
- **Torsades de pointes-inducing agents: class Ia antiarrhythmic active substances (quinidine, hydroquinidine, disopyramide and procainamide) and class III antiarrhythmic active substances (amiodarone, dofetilide, ibutilide…), some neuroleptics (thioridazine, chlorpromazine, levomepromazine, trifluoperazine, cyamemazine, sulpiride, sultopride, amisulpride, tiapride, pimozide, haloperidol, droperidol…), bepridil, cisapride, diphemanil, erythomycin IV, mizolastine, vincamine IV, moxifloxacin …**

  Increased risk of ventricular arrhythmias, particularly torsades de pointes.

Combinations not recommended

- **Halofantrine, pentamidine, fluoroquinolones, methadone**: increased risk of ventricular arrhythmias, particularly torsades de pointes.

  If possible, the torsades de pointes-inducing medicinal product should be discontinued, unless it is an anti-infective agent. If the combination is unavoidable, the QT interval should be measured beforehand and the ECG monitored.
- **Diltiazem, verapamil**:

  As with other beta-blockers, automatism disorders (excessive bradycardia, sinus arrest), sinoatrial and atrioventricular conduction disorders, heart failure (effect synergy) may occur. Such a combination should only be used with close clinical and ECG monitoring, especially in the elderly, and at the initiation of therapy.
- Drugs which can induce hypertension (e.g. MAOIs).

Associations requiring precautions for use

- **Active substances causing hypokaleamia (potassium-depleting diuretics, stimulant laxatives, glucocorticoids, tetracosactide, amphotericin B (IV))**: increased risk of ventricular arrhythmias, in particular torsades de pointes.

  Any decrease in potassium levels should be corrected before the product is administered. Clinical, electrolytic and ECG monitoring is necessary.
- **Bradycardia-inducing active substances (bradycardia-inducing calcium antagonists: diltiazem, verapamil; centrally-acting antihypertensive agents such as clonidine, guanfacine, alpha-methyldopa; digitalis glycosides including digoxin; class Ia and Ic antiarrhythmic agents; mefloquine; cholinesterase inhibitors such as those used in Alzheimer's disease e.g. donepezil, rivastigmine, tacrine, galantamine, neostigmine, pyridostigmine, ambenonium; pilocarpine, other beta-blocking agents)**

  Increased risk of ventricular arrhythmias, in particular torsades de pointes, due to the torsades de pointes-inducing properties of sotalol.

  Clinical and ECG monitoring required.

  Additionally, for centrally-acting antihypertensive agents, rebound hypertension may occur if they are withdrawn abruptly.
- **Volatile halogenated anaesthetics**: Sotalol reduces the compensatory cardiovascular response (beta-agonists may be used during the procedure to overcome the beta-blockade).

  As a general rule, sotalol should not be withdrawn, and must never be discontinued abruptly.

  The anaesthetist must be informed that the patient is receiving sotalol.
- **Insulin, hypoglycaemic sulphonamides**: All beta-blockers can mask certain symptoms of hypoglycaemia: palpitations and tachycardia. Most non-cardioselective beta-blockers increase the incidence and severity of hypoglycaemia.

  Inform the patient and reinforce self-monitoring of the blood, especially at the initiation of therapy.
- **Propafenone**: Contractility, automatism and conduction disorders (inhibition of compensatory sympathetic mechanisms).

  Clinical and ECG monitoring required.
- **Baclofen**: Increased antihypertensive effect.

Blood pressure should be monitored and the antihypertensive dosage adjusted if necessary.

- **Lidocaine (administered intravenously)**: Increased lidocaine plasma levels, with possible cardiac and neurological adverse effects (decreased hepatic clearance of lidocaine).
  Clinical and ECG monitoring required.
- **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.
- **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.

Associations to be taken into account:

- **NSAIDs** (extrapolated from indomethacin): Decreased antihypertensive effect (NSAIDs inhibited the vasodilator prostaglandins; pyrazole NSAIDs cause sodium and water retention).
- **Imipramine antidepressants (tricyclics), phenothiazine neuroleptics, amifostine**: Increased antihypertensive effect and risk of orthostatic hypotension (additive effect).
- **Calcium channel-blocking active substances (dihydropyridines)**: hypotension, conduction defects, bradycardia, cardiac failure in patients with latent or uncontrolled cardiac failure (negative inotropic effect of dihydropyridines (in vitro), more or less marked depending on the product, and prone to add to the negative inotropic effect of sotalol). The presence of sotalol can also minimise the sympathetic reflex reaction arising due to excessive haemodynamic repercussion.
- **Dipyridamole (administered intravenously)**: Increased antihypertensive effect.
- **Interactions with laboratory tests:**
  The presence of sotalol in the urine may result in falsely elevated levels of urinary metanephrine, when measured by a photometric method. The urine of sotalol-treated patients suspected of having phaeochromocytoma should be analysed using the HPLC assay with solid phase extraction.
- Athletes should be warned of the fact that this medicine contains an active substance which can induce a positive reaction in drug tests.

4.6. Fertility, pregnancy and lactation

Pregnancy

There are no well-controlled studies on the use of sotalol in pregnant women. Animal studies with sotalol hydrochloride have shown no evidence of teratogenicity or other harmful effects on the foetus after use of sotalol at therapeutic doses

In humans, sotalol crosses the placenta. Due to its pharmacological properties, adverse effects may occur in the foetus and neonate, after use of sotalol later in pregnancy.

In neonates born to mothers treated with sotalol, the beta-blocking action of the drug can still be present several days after birth. It may manifest as bradycardia, respiratory distress or hypoglycaemia. In general, this fact is clinically insignificant. However, it is possible that, by reducing compensatory cardiovascular reactions, cardiac failure requiring hospitalisation and intensive care may occur (see section 4.9). In such cases, plasma expanders should be avoided (risk of acute pulmonary oedema).

Consequently, sotalol may be administered during pregnancy only if needed. The neonate should be monitored very carefully for 48-72 hours after delivery if it was not possible to terminate maternal therapy with sotalol 2-3 days before the birth date.

Breast-feeding
Sotalol is transferred to breast milk in relatively large quantities.
Hypoglycaemia and bradycardia have been reported to occur in breast-fed children whose mothers are treated with some beta-blockers that bind little to plasma proteins. Consequently, breast-feeding is not recommended during the course of treatment.

4.7. Effects on ability to drive and use machines

Sotalol can influence individual reactions to such an extent that the ability to take an active part in road traffic or to operate machines or work without suitable safeguards may be impaired.

4.8. Undesirable effects

Clinical
The most frequent undesirable effects of sotalol arise from its beta-blockade properties. They are usually transient in nature, and rarely require discontinuation of the treatment. They usually disappear when the dosage is reduced. The most serious undesirable effects are those due to proarrhythmic effects, including torsades de pointes (see section 4.4).

Frequency is defined using the following convention: not known (cannot be estimated from the available data)

The most frequent undesirable effects are:
- ***Blood and lymphatic system disorders***: thrombocytopenia, eosinophilia, leucopenia;
- ***Metabolism and nutrition disorders***: hypoglycaemia;
- ***Psychiatric disorders***: depression, anxiety, mood altered;
- ***Nervous system disorders***: dizziness, headaches, sleep disturbances, paraesthesia, fatigue, asthenia, lightheadedness, dysgeusia;
- ***Eye disorders***: visual disorders;
- ***Cardiac disorders:*** sinus bradycardia, atrioventricular conduction disorders, chest pain, palpitations, ECG abnormalities, proarrhythmia, heart failure;
- ***Vascular disorders:*** oedema, hypotension, syncope, presyncope, Raynaud's syndrome; aggravation of existing intermittent claudication;
- ***Respiratory, thoracic and mediastinal disorders***: bronchonconstriction, dyspnoea, in particular in patients with obstructive ventilation disorders;
- ***Gastrointestinal disorders***: nausea, vomiting, diarrhoea, dyspepsia, abdominal pain, flatulence;
- ***Skin and subcutaneous tissue disorders***: various cutaneous manifestations, including psoriasis-like eruptions or exacerbation of psoriasis (see section 4.4), exanthema, rash, pruritus, photosensitivity, diaphoresis, alopecia, hyperhidrosis;
- ***Musculoskeletal and connective tissue disorders***: cramps, arthralgia, myalgia;
- ***Reproductive system and breast disorders***: disorders of sexual function;
- ***General disorders and administration site conditions***: fever.
- ***Ear and labyrinth disorders***: hearing disturbances.

Investigations
In rare cases, formation of anti-nuclear anti-bodies has been reported, only exceptionally accompanied by clinical manifestations of lupus-like syndrome which disappear when the treatment is discontinued.

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

Accidental or intentional overdosage with sotalol has rarely resulted in death. Haemodialysis results in a large reduction of plasma levels of sotalol.
The commonest signs of overdose are as follows: bradycardia, congestive heart failure, hypotension, bronchospasm, hypoglycaemia.
In cases of massive intentional overdosage (2-16 g) of sotalol, the following clinical findings have been reported: hypotension, bradycardia, atrioventricular heart block, QT interval prolongation, premature ventricular complexes, ventricular tachycardia, torsades de pointes.
In case of:

- bradycardia or excessive decrease in blood pressure, 0.5-2 mg IV atropine and 1 mg glucagon should be administered, followed if necessary by a slow injection of 25 micrograms isoprenaline or 2.5-10 micrograms/kg/min dobutamine. Further doses of glucagon may be administered if necessary;
- 2nd or 3rd degree atrioventricular block: treatment by transmural cardiac pacing;
- bronchospasm: treatment with theophylline or β_2-receptor-stimulant aerosol.
- Torsades de pointes: treatment with cardioversion, transmural cardiac pacing and/or magnesium sulphate.

In case of cardiac decompensation in neonates, where the mother was being treated with sotalol:

- 0.3 mg/kg glucagon;
- hospitalisation in intensive care;
- isoprenaline and dobutamine: as the posologies are generally high and the treatment prolonged, specialised monitoring is necessary (see section 4.6).

Overdose is associated with a risk of serious ventricular arrhythmias (torsades de pointes).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Beta-blocking agents, non-selective – Sotalol, ATC code: C07A A07

Sotalol is an antiarrhythmic agent with both class II properties (non-selective beta-adrenergic receptor blocking agent, devoid of intrinsic sympathomimetic activity or membrane stabilising activity) and class III properties (prolongation of duration of cardiac action potential). Sotalol has no known effect on the upstroke velocity and therefore no effect on the depolarisation phase.

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 25mg, Class III effects are usually seen at daily doses of greater than 160mg.

Its β-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 β-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.

Electrophysiology
Sotalol decreases heart rate and atrioventricular conduction velocity (PR interval prolongation), increases the refractory period of the atrioventricular junction, increases QT & QTc intervals, without altering ventricular depolarisation (no significant changes in QRS duration). It prolongs the atrial, ventricular and accessory pathway refractory periods (in the anterograde and retrograde directions).

Haemodynamics
Due to its beta-blockade properties, sotalol has negative inotropic effects. Conversely, its class III properties cause a positive inotropic effect. Even though sotalol is usually well tolerated from a haemodynamic point of view, caution is recommended in the presence of altered ventricular function.
Like other beta-blockers, sotalol produces a reduction in both systolic and diastolic blood pressure in hypertensive patients.

5.2. Pharmacokinetic properties

Absorption
The maximum plasma concentration is reached in 2.5 to 4 hours after oral administration and the plasma steady state is reached in 2 to 3 days. Bioavailability is greater than 90% and shows very little inter-individual variation. Good correlation can be noted between the dose administered and the plasma concentrations. Bioavailability is reduced by approximately 20 % when the product is administered with a meal.

Distribution
The apparent volume of distribution is 1.2 to 2.4 l/kg. Protein binding is negligible, facilitating tissue diffusion of sotalol.
Penetration across the blood-brain barrier is poor (cerebrospinal fluid concentration < 10% of plasma concentration).

Passage across the placental barrier
Sotalol passes the placental barrier. The ratio between the umbilical cord blood concentration and the maternal blood concentration is 1.05/1.
Excretion in milk is high. The ratio between the concentration in the mother's milk and plasma is 5/1.

Biotransformation
Sotalol is not metabolised.

Plasma half-life
10 to 20 hours in a subject with normal renal function.

Elimination
Sotalol is eliminated by renal excretion. Approximately 80 to 90% of the dose administered is excreted unchanged in the urine. Dosage adjustment is necessary in conditions of renal impairment (see section 4.2).
Age does not significantly change the pharmacokinetic parameters even though renal function in geriatric patients may decrease elimination, resulting in increased accumulation of sotalol.

5.3. Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Maize starch
Indigo carmine (E132)
Povidone (K30)
Magnesium stearate

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

3 years

6.4. Special precautions for storage

Keep the blister in the outer carton in order to protect from light.

6.5. Nature and contents of container

80 mg:
PVC/PVdC/aluminium blisters containing 20, 28, 30, 40, 50, 60, 90 and 100 scored tablets. 50 tablets in EAV blisters (hospital packs)

Not all pack sizes may be marketed.

6.6. Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

UK: Teva UK Limited
Ridings Point, Whistler Drive,
Castleford, WF10 5HX, United Kingdom

8. MARKETING AUTHORISATION NUMBER(S)

PL 00289/0389

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

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12/07/2022