Sotalol hydrochloride tablets, USP

**DESCRIPTION**

Sotalol hydrochloride tablets contain the active ingredient: sotalol hydrochloride, a selective beta-blocking agent. This agent is indicated for the maintenance of normal sinus rhythm [delay in time to recurrence of atrial fibrillation/flutter (AFIB/AFL)] in patients with symptomatic AFIB/AFL who are currently in sinus rhythm and is effective in reducing the incidence of AFIB/AFL after cardioversion.

**CLINICAL PHARMACOLOGY**

**Absorption**

Sotalol hydrochloride tablets are readily absorbed after oral administration. Peak plasma levels are usually reached within 3 hours. Oral absorption is rapid and complete, and peak plasma levels occur within 1–3 hours.

**Distribution**

Sotalol hydrochloride is extensively distributed to all tissues and extracellular fluids. Sotalol distributes largely to the extravascular volume, with a mean apparent volume of distribution of approximately 70 liters in adults. In the elderly, the mean apparent volume of distribution is approximately 80 liters.

**Metabolism**

Sotalol hydrochloride is primarily metabolized by the cytochrome P450 3A4 (CYP3A4) enzyme system in the liver. Sotalol is extensively metabolized (approximately 90%–100% of an oral dose) to 3’-hydroxy-sotalol, which is the major circulating metabolite. The disposition of 3’-hydroxy-sotalol in plasma is similar to that of sotalol hydrochloride. Sotalol hydrochloride displays dose proportionality with respect to plasma concentrations.

**Elimination**

The mean plasma elimination half-life of sotalol is 9–12 hours in adults and 12–17 hours in the elderly (≥65 years of age). The terminal half-life of 3’-hydroxy-sotalol is approximately 21 hours in adults and 28–37 hours in the elderly (≥65 years of age). The renal clearance of sotalol hydrochloride is about 40% of the apparent plasma clearance in adults and increases with age. The renal clearance of sotalol hydrochloride is approximately 50% in the elderly (≥65 years of age). The renal clearance of 3’-hydroxy-sotalol is approximately 30% in adults and 35% in the elderly (≥65 years of age).

**Special Populations**

**Elderly**

In the elderly, the mean apparent volume of distribution is approximately 80 liters.

**Children**

The safety and effectiveness of sotalol hydrochloride have not been established in children.

**INTERACTIONS**

Sotalol hydrochloride may increase plasma concentrations of theophylline and warfarin, and decrease plasma concentrations of diazepam and diazepam metabolites. Sotalol may decrease the clearance of theophylline and may potentiate warfarin’s anticoagulant effect. Sotalol may increase the clearance of diazepam and its metabolites.

**INDICATIONS AND USAGE**

Sotalol hydrochloride tablets are indicated for the maintenance of normal sinus rhythm [delay in time to recurrence of atrial fibrillation/flutter (AFIB/AFL)] in patients with symptomatic AFIB/AFL who are currently in sinus rhythm and is effective in reducing the incidence of AFIB/AFL after cardioversion.

**CONTRAINDICATIONS**

Sotalol hydrochloride tablets are contraindicated in patients with symptomatic atrial fibrillation/flutter (AFIB/AFL) who are in the atrial fibrillation/flutter (AFIB/AFL) state or those with atrial fibrillation/flutter (AFIB/AFL) who are in the atrial flutter (AFL) state or those with atrial fibrillation/flutter (AFIB/AFL) who are in the atrial fibrillation/flutter (AFIB/AFL) state and who require an anticoagulant drug. Sotalol is contraindicated in patients with symptomatic atrial fibrillation/flutter (AFIB/AFL) who are in the atrial flutter (AFL) state or those with atrial fibrillation/flutter (AFIB/AFL) who are in the atrial fibrillation/flutter (AFIB/AFL) state and who require an anticoagulant drug. Sotalol is contraindicated in patients with symptomatic atrial fibrillation/flutter (AFIB/AFL) who are in the atrial flutter (AFL) state or those with atrial fibrillation/flutter (AFIB/AFL) who are in the atrial fibrillation/flutter (AFIB/AFL) state and who require an anticoagulant drug.

**WARNINGS**

**Heart Failure**

Sotalol hydrochloride tablets are contraindicated in patients with severe heart failure (NYHA Class III or IV) or in patients who are receiving concomitant therapy with a catecholamine depletor (e.g., clonidine or guanethidine) or who have a history of congestive heart failure (CHF) or who have a history of AFIB/AFL who are in the atrial fibrillation/flutter (AFIB/AFL) state or those with atrial fibrillation/flutter (AFIB/AFL) who are in the atrial flutter (AFL) state or those with atrial fibrillation/flutter (AFIB/AFL) who are in the atrial fibrillation/flutter (AFIB/AFL) state and who require an anticoagulant drug.

**Cardiac Conduction**

Sotalol hydrochloride tablets are contraindicated in patients with symptomatic atrial fibrillation/flutter (AFIB/AFL) who are in the atrial flutter (AFL) state or those with atrial fibrillation/flutter (AFIB/AFL) who are in the atrial fibrillation/flutter (AFIB/AFL) state and who require an anticoagulant drug.

**PRECAUTIONS**

**Hypokalemia and/or Hypomagnesemia**

Sotalol hydrochloride tablets are contraindicated in patients with symptomatic atrial fibrillation/flutter (AFIB/AFL) who are in the atrial flutter (AFL) state or those with atrial fibrillation/flutter (AFIB/AFL) who are in the atrial fibrillation/flutter (AFIB/AFL) state and who require an anticoagulant drug.

**Electrolyte Abnormalities**

Sotalol hydrochloride tablets are contraindicated in patients with symptomatic atrial fibrillation/flutter (AFIB/AFL) who are in the atrial flutter (AFL) state or those with atrial fibrillation/flutter (AFIB/AFL) who are in the atrial fibrillation/flutter (AFIB/AFL) state and who require an anticoagulant drug.

**RENAL IMPAIRMENT**

Sotalol hydrochloride tablets are contraindicated in patients with symptomatic atrial fibrillation/flutter (AFIB/AFL) who are in the atrial flutter (AFL) state or those with atrial fibrillation/flutter (AFIB/AFL) who are in the atrial fibrillation/flutter (AFIB/AFL) state and who require an anticoagulant drug.

**PREGNANCY**

Sotalol hydrochloride tablets are contraindicated in patients with symptomatic atrial fibrillation/flutter (AFIB/AFL) who are in the atrial flutter (AFL) state or those with atrial fibrillation/flutter (AFIB/AFL) who are in the atrial fibrillation/flutter (AFIB/AFL) state and who require an anticoagulant drug.

**NURSING MOTHERS**

Sotalol hydrochloride tablets are contraindicated in patients with symptomatic atrial fibrillation/flutter (AFIB/AFL) who are in the atrial flutter (AFL) state or those with atrial fibrillation/flutter (AFIB/AFL) who are in the atrial fibrillation/flutter (AFIB/AFL) state and who require an anticoagulant drug.

**ADVERSE REACTIONS**

**OVERDOSE**

In patients with diabetes (especially tight diabetes control) and with a history of episodes of spontaneous hypoglycemia, sotalol hydrochloride may add to the potentially serious consequences of such hypoglycemia, e.g., thycauria.

**SIDE EFFECTS**

Sotalol should be used with particular caution if the QTc is greater than 500 m sec on-therapy and if the QTc is greater than 500 m sec on-therapy. Nonetheless, sotalol should be used with particular caution if the QTc is greater than 500 m sec on-therapy and if the QTc is greater than 500 m sec on-therapy.


**INDICATIONS AND USAGE**

Sotalol hydrochloride must be individualized for each patient on the basis of therapeutic response and tolerance. Dosage increments should be made at 3-day intervals. Initial doses of 20 to 40 mg/m² of body surface area are recommended in adults. The initial dose may be increased gradually, in the absence of toxicity, by 20 mg/m² on days 3 and 7, until a maintenance dose is reached. If additional antihypertensive effects are required, the addition of a diuretic may be needed.

**OVERDOSAGE**

The most common signs to be expected are bradycardia, congestive heart failure, hypotension, bronchospasm, and shock. In patients with sotalol and/or betablocker overdosage, the following signs should be observed: tachycardia, hypotension, hypoxemia, cyanosis, bradycardia, widening of the QRS complex, decreased cardiac output, minimal or absent peripheral pulses, and QRS widening.

**DOSING**

**Adults**

Sotalol hydrochloride syrup 5 mg/mL can be compounded using Simple Syrup containing 0.1% sodium benzoate and 0.1% citric acid. The solution is stable for 30 days when stored at room temperature.

**Children**

For children aged 2 years and greater, recommended dosages are similar to adults; for children aged less than 2 years, the dose should be adjusted according to body weight and body surface area. For infants aged less than 2 months, the dose should be adjusted to body weight.

**Drug Interactions**

Sotalol should be used cautiously in patients with impaired renal function or impaired hepatic function, because the half-life of the drug is prolonged. It may be necessary to reduce the dose or frequency of administration to avoid the development of toxicity.

**Special Concerns**

Sotalol may produce a slight decrease in systolic blood pressure, particularly in patients with coronary artery disease, and it may occasionally cause an increase in diastolic blood pressure.

**Precautions**

Sotalol should be used with caution in patients with a history of gastrointestinal disease, including peptic ulcer disease, because it may increase the risk of bleeding. It should also be used with caution in patients with a history of renal impairment, because it may increase the risk of renal failure.

**Adverse Reactions**

The most common adverse reactions associated with sotalol therapy are headache, dizziness, and fatigue. Other adverse reactions include nausea, vomiting, diarrhea, constipation, skin rash, pruritus, and phlebitis. In addition, sotalol may cause a decrease in cardiac output, which may be associated with a decrease in blood pressure.

**Pharmacology**

Sotalol is a non-selective beta-blocker with weak intrinsic sympathomimetic activity. It is a competitive inhibitor of beta-adrenergic receptors, with a high affinity for beta-1 receptors. It also has properties of a class III antiarrhythmic agent, which may help to prolong the refractory period of the atrioventricular node and prevent the occurrence of atrioventricular conduction blocks.

**Clinical Studies**

In clinical studies, sotalol has been shown to be effective in treating a variety of arrhythmias, including atrial fibrillation, atrial flutter, and supraventricular tachycardia. It has also been shown to be effective in preventing the recurrence of these arrhythmias after cardioversion or catheter ablation.

**Dosage and Administration**

Initial dosing should be 20 to 40 mg/m² of body surface area given twice daily. The dose may be increased gradually, in the absence of toxicity, by 20 mg/m² on days 3 and 7, until a maintenance dose is reached. If additional antihypertensive effects are required, the addition of a diuretic may be needed.

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