AURORA REMEDIES

SIBUTRAMINE HYDROCHLORIDE

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Sibutramine Hydrochloride is an orally administered agent for the treatment of obesity.

Chemical: Sibutramine Hydrochloride
CAS Name: 1-[1-(4-chlorophenyl)cyclobutyl]-N,N,3-trimethylbutan-1-amine;hydrate;hydrochloride
Molecular Formula: C17H29CL2NO
Molecular Weight: 334.32.

Prescription Medicine

CLINICAL PHARMACOLOGY

Mode of Action
Sibutramine produces its therapeutic effects by norepinephrine, serotonin and dopamine reuptake inhibition. Sibutramine and its major pharmacologically active metabolites (M1 and M2) do not act via release of monoamines.
Pharmacodynamics
Sibutramine exerts its pharmacological actions predominantly via its secondary (M1) and primary (M2) amine metabolites. The parent compound, sibutramine, is a potent inhibitor of serotonin (5-hydroxytryptamine, 5-HT) and norepinephrine reuptake in vivo, but not in vitro . However, metabolites M1 and M2 inhibit the reuptake of these neurotransmitters both in vitro and in vivo.
In human brain tissue, M1 and M2 also inhibit dopamine reuptake in vitro , but with ~3-fold lower potency than for the reuptake inhibition of serotonin or norepinephrine.

INDICATIONS AND USAGE

Sibutramine hydrochloride is indicated for the management of obesity, including weight loss and maintenance of weight loss, and should be used in conjunction with a reduced calorie diet.
Sibutramine is recommended for obese patients with an initial body mass index ≥ 30 kg/m², or ≥ 27 kg/m² in the presence of other risk factors (e.g., diabetes, dyslipidemia, controlled hypertension).

CONTRAINDICATIONS

Sibutramine hydrochloride is contraindicated in patients:
-with a history of coronary artery disease (e.g., angina, history of myocardial infarction), congestive heart failure, tachycardia, peripheral arterial occlusive disease, arrhythmia or cerebrovascular disease (stroke or transient ischemic attack (TIA)).
- with inadequately controlled hypertension > 145/90 mm Hg.
- over 65 years of age.
- receiving monoamine oxidase inhibitors (MAOIs).
- with hypersensitivity to sibutramine or any of the inactive ingredients of Sibutramine Hydrochloride.
- who have a major eating disorder (anorexia nervosa or bulimia nervosa).
- taking other centrally acting weight loss drugs.

PRECAUTIONS

Pulmonary Hypertension
Certain centrally-acting weight loss agents that cause release of serotonin from nerve terminals have been associated with pulmonary hypertension (PPH), a rare but lethal disease. In premarketing clinical studies, no cases of PPH have been reported with sibutramine tablets. Because of the low incidence of this disease in the underlying population, however, it is not known whether or not sibutramine hydrochloride may cause this disease.
Seizures
During premarketing testing, seizures were reported in < 0.1% of sibutramine treated patients. Sibutramine hydrochloride should be used cautiously in patients with a history of seizures. It should be discontinued in any patient who develops seizures.
Bleeding
There have been reports of bleeding in patients taking sibutramine. While a causal relationship is unclear, caution is advised in patients predisposed to bleeding events and those taking concomitant medications known to affect hemostasis or platelet function.
Gallstones
Weight loss can precipitate or exacerbate gallstone formation.
Renal Impairment
Sibutramine hydrochloride should be used with caution in patients with mild to moderate renal impairment. Sibutramine hydrochloride monohydrate should not be used in patients with severe renal impairment, including those with end stage renal disease on dialysis.
Hepatic Dysfunction
Patients with severe hepatic dysfunction have not been systematically studied; sibutramine hydrochloride should therefore not be used in such patients.

ADVERSE REACTIONS

The following additional adverse events were reported in ≥ 1% of all patients who received sibutramine in controlled and uncontrolled premarketing studies.
Body as a Whole: fever.
Digestive System : diarrhea, flatulence, gastroenteritis, tooth disorder.
Metabolic and Nutritional: peripheral edema.
Musculoskeletal System: arthritis.
Nervous System: agitation, leg cramps, hypertonia, thinking abnormal.
Respiratory System: bronchitis, dyspnea.
Skin and Appendages: pruritus.
Special Senses: amblyopia.
Urogenital System: menstrual disorders.
Other Adverse Events
Clinical Studies
Seizures
Convulsions were reported as an adverse event in three of 2068 (0.1%) sibutramine treated patients and in none of 884 placebo-treated patients in placebo-cont rolled premarketing obesity studies. Two of the three patients with seizures had potentially predisposing factors (one had a prior history of epilepsy; one had a subsequent diagnosis of brain tumor). The incidence in all subjects who received sibutramine (three of 4,588 subjects) was less than 0.1%.
Ecchymosis/Bleeding Disorders
Ecchymosis (bruising) was observed in 0.7% of sibutramine trea ted patients and in 0.2% of placebo-treated patients in premarketing placebo-controlled obesity studies. One patient had prolonged bleeding of a small amount which occurred during minor facial surgery. Sibutramine may have an effect on platelet function due to its effect on serotonin uptake.
Interstitial Nephritis
Acute interstitial nephritis (confirmed by biopsy) was reported in one obese patient receiving sibutramine during premarketing studies. After discontinuation of the medication, dialysis and oral corticosteroids were administered; renal function normalized. The patient made a full recovery.

DOSAGE AND ADMINISTRATION

The recommended starting dose of sibutramine hydrochloride is10 mg administered once daily with or without food. If there is inadequate weight loss, the dose may be titrated after four weeks to a total of 15 mg once daily. The 5 mg dose should be reserved for patients who do not tolerate the 10 mg dose. Blood pressure and heart rate changes should be taken into account when making decisions regarding dose titration.
Doses above 15 mg daily are not recommended. In most of the clinical trials, sibutramine hydrochloride monohydrate was given in the morning.
Analysis of numerous variable s has indicated that approximately 60% of patients who lose at least 4 pounds in the first 4 weeks of treatment with a given dose of sibutramine hydrochloride monohydrate in combination with a reduced-calorie diet lose at least 5% (placebo-subtracted) of their initial body weight by the end of 6 months to 1 year of treatment on that dose of sibutramine hydrochloride monohydrate. Conversely, approximately 80% of patients who do not lose at least 4 pounds in the first 4 weeks of treatment with a given dose of sibutramine hydrochloride do not lose at least 5% (placebo-subtracted) of their initial body weight by the end of 6 months to 1 year of treatment on that dose. If a patient has not lost at least 4 pounds in the first 4 weeks of treatment, the physician should consider reevaluation of therapy which may include increasing the dose or discontinuation of sibutramine.

STORAGE

Store at room temperature between 59-86 degrees Fahrenheit (15-30 degrees Celsius), away from light and moisture. Do not store in the bathroom. Keep all medicines away from children and pets.Do not flush medications down the toilet or pour them into a drain unless instructed to do so. Properly discard this product when it is expired or no longer needed. Consult your pharmacist or local waste disposal company for more details about how to safely discard your product.

PRESENTATION:

20mg tablets in blister packs of 10 tablets – 10 blisters per box (100 tablets).

AURORA REMEDIES, SINGAPORE
www.aurora-remedies.com