Obestat | Sibutramine hydrochloride monohydrate

Sibutramine is a centrally acting **anorexiant** formerly used in the management of **obesity**, particularly in patients with a **BMI ?30 kg/m²** or **?27 kg/m²** with comorbid conditions (e.g., type 2 diabetes, dyslipidemia, or hypertension). It was **withdrawn in many countries**, including the U.S. and EU, due to increased cardiovascular risks.

Mechanism of Action

- **Centrally acting sympathomimetic** agent.
- Inhibits the **reuptake of serotonin (5-HT), norepinephrine (NE), and dopamine (DA)** in the hypothalamus.
- Increases **satiety** and decreases appetite.
- Secondary effects: Enhances **thermogenesis** and increases **energy expenditure** via sympathetic stimulation.

Clinical Effects

- Promotes **dose-dependent weight loss**.
- Reduces **waist circumference** and **visceral fat**.
- Improves lipid profile:
  - ? Triglycerides, ? VLDL
  - ? HDL
- Enhances **insulin sensitivity** and **glucose metabolism**.

NOTE:

Due to **adverse cardiovascular effects**, sibutramine has been **withdrawn from most markets** (FDA withdrawal in 2010).

Pharmacokinetics

- **Route**: Oral
- **Absorption**: Well-absorbed, undergoes **first-pass metabolism** in the liver.
- **Active Metabolites**: Desmethylsibutramine and didesmethylsibutramine.
- **Elimination**: Metabolites excreted in **urine (85%)** and **feces**.
- **Half-life**: Active metabolites ~14–16 hours.

Dosage

Patient Group	Recommended Dose
Adults	Initial: 10 mg once daily. May increase to 15 mg/day after 4 weeks if no adequate response.
Special cases	5 mg for patients intolerant to 10 mg

Patient Group	Recommended Dose
Max dose	15 mg/day
Pediatrics	Not approved for <16 years

Indications

- Adjunct to a **reduced-calorie diet** for:
  - Obese adults (BMI ?30)
  - Overweight adults (BMI ?27) with associated risk factors.

Contraindications

- **Uncontrolled hypertension**
- **Cardiovascular diseases** : CAD, CHF, arrhythmias, stroke
- **Hyperthyroidism**
- **Glaucoma**
- **History of eating disorders**
- **MAOI use within 14 days**
- **Pregnancy and lactation**
- **Age <16 years**

Precautions

- Regular **BP and HR monitoring** .
- Avoid in patients with **renal impairment** or **hepatic dysfunction** .
- Monitor for **psychiatric symptoms** : agitation, depression, suicidal ideation.
- **Abuse potential** : May cause **tolerance and dependence** .

Adverse Effects

Common:

- **Dry mouth**
- **Constipation**
- **Insomnia**
- **Headache**
- **Increased BP and HR**

Serious:

- **Seizures**
- **Arrhythmias**
- **Hypertensive crisis**
- **Serotonin syndrome** (when combined with SSRIs, SNRIs, MAOIs, or triptans)
- **Psychiatric symptoms** : depression, agitation, suicidal thoughts

Drug Interactions

- **SSRIs, SNRIs, MAOIs** ? ? risk of serotonin syndrome
- **CYP3A4 inhibitors/inducers** ? altered sibutramine metabolism
- **Triptans, ergotamine** , **decongestants** ? ? hypertensive risk
- **St. John’s Wort** and **other serotonergic agents** should be avoided

Use in Pregnancy and Lactation

- **Pregnancy Category C**
- Not recommended during **pregnancy** or **breastfeeding**
- Effective **contraception** advised during use

Pediatric Use

- **Not recommended** for patients <16 years due to increased **psychiatric side effects** and lack of safety data

Availability

Note : Sibutramine has been withdrawn in many regions
Previously available as capsules :

- 5 mg
- 10 mg
- 15 mg

Evidence-Based Findings

- A **meta-analysis** (Padwal et al., 2003) reported:
  - **4.6% mean weight loss** over one year
  - **15% of patients** lost ?10% of body weight
  - Significant improvements in **lipid profile** and **waist circumference**