

# Emerging Drug List

## SIBUTRAMINE



- Generic (Trade Name):** Sibutramine (Meridia®)
- Manufacturer:** Knoll Pharma Inc. (Markham, ON)
- Indication:** For the management of obesity, including weight loss and maintenance of weight loss, in conjunction with a reduced calorie diet.
- Current Regulatory Status:** Knoll Pharma Inc. received a Notice of Compliance from Health Canada in January 2001 and the company launched the product on April 2, 2001. They have also developed a patient support program, The New Menu for Life™, to assist with weight management. Sibutramine has been available on the U.S. market since January 1998.
- Description:** Sibutramine is a beta-phenylethylamine that exhibits monoamine reuptake-inhibitor activity for norepinephrine, serotonin, and to a lesser extent, dopamine. The precise mechanism by which sibutramine acts as an anorexiant is not known. However, sibutramine is believed to act by decreasing food/energy intake or increasing energy expenditure, or a combination of both. The recommended starting dose is 10 mg daily. If, after four weeks, the desired effects are not achieved, the dose can be increased to 15 mg daily. Patients who do not tolerate the 10 mg dose can have the dose reduced to 5 mg daily. Meridia® is available in capsule form in two strengths (i.e., 10 mg, and 15 mg).
- Current Existing Treatment:** Medications that are currently approved in Canada for obesity include the gastrointestinal lipase inhibitor orlistat (Xenical® by Hoffman LaRoche), the amphetamine-like appetite suppressants diethylpropion (Tenuate® and Tenuate® Dospan by Aventis Pharma), mazindol (Sanorex® by Novartis), and phentermine (Ionamin® by Aventis Pharma). Although not approved as an anorexiant, fluoxetine (Prozac® by Eli Lilly) has been studied for this condition and is used in clinical practice for obesity.
- Cost:** The wholesale price for sibutramine is \$98.40 for the 10 mg capsules and \$113.40 for the 15 mg capsules (bottles of 30). Hence a month supply of sibutramine would range from \$98.40 to \$113.40 (without dispensing fees and other mark-ups).
- Evidence:** The safety and efficacy of sibutramine have been evaluated in double-blind, placebo or active-controlled trials. The doses that have been evaluated ranged from 1 to 30 mg/day. Most studies included obese adults from 18 to 65 years of age with a body mass index (BMI) between 27 and 40 kg/m<sup>2</sup>. In the largest study, 1024 patients who received either placebo or various doses of sibutramine (1-30 mg/day) were followed for 24 weeks. The mean percent reduction in weight for the various groups was 0.9%



**Evidence (con't)** (placebo), 1.9% (1 mg), 3.1% (5 mg), 4.7% (10 mg), 5.8% (15 mg), 6.6% (20 mg), and 7.7% (30 mg). The percentage of patients who lost more than five percent of their initial body mass was 13% (placebo), 19% (1 mg), 32% (5 mg), 45% (10 mg), 53% (15 mg), 52% (20 mg), 63% (30 mg).

The results of a long-term study (1 year, n=246) showed that the percentage of patients who lost more than five percent of initial body mass was 20.4% (placebo), 40.0% (10 mg), and 56.9% (15 mg). Another long-term study (1 year, n=82) showed a mean increase in baseline weight of 0.5% in the placebo group and a mean decrease of 5.2% in patients receiving 10 mg daily of sibutramine.

**Adverse Effects:** The most commonly reported adverse effects in clinical trials included dry mouth, anorexia, insomnia, constipation, and headache. Sibutramine was also associated with a mean increase in blood pressure of 1-3 mmHg and heart rate of 4-5 beats/min.

**Conclusion:** Sibutramine is the first agent of this class approved in Canada for the treatment of obesity. It is effective in the management of obesity when used in conjunction with a calorie-restricted diet. It should also be used in conjunction with behaviour and lifestyle modifications. Patients with certain concomitant diseases (e.g., coronary artery disease, congestive heart failure, arrhythmias, stroke) should not use sibutramine because of its ability to increase heart rate and blood pressure.

- References:**
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  2. Kolanowski J. A risk-benefit assessment of anti-obesity drugs. *Drug Safety* 1999;20(2):119-31.
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  4. Bray GA, Blackburn CL, Ferguson JM et al. Sibutramine produced dose-related weight loss. *Obes Res* 1999;7:189-98.
  5. Jones SP, Heath MJ. Long term weight loss with sibutramine: 5% responders (abstract). *Int J Obes Relat Metab Disord* 1996;20(suppl 4):157.
  6. Apfelbaum M, Vague P, Ziegler O et al. Long-term maintenance of weight loss after a very-low-calorie diet: a randomized blinded trial of the efficacy and tolerability of sibutramine. *Am J Med* 1999;106:179-84.

The contents of this bulletin are current as of April 2001.

The Emerging Drug List highlights drugs not yet approved in Canada that are anticipated to have a significant impact on the health care system. Minimal information is available about these drugs, and they may in future become the subject of an early assessment.

ISSN # 1496-8398