CVD Contraindication Added to Sibutramine

BY ELIZABETH MECHCATIE

The weight-loss drug sibutramine is now contraindicated in people with a history of cardiovascular disease, the Food and Drug Administration announced last month.

The recommendation was based on a review of data indicating an increased risk of myocardial infarction and stroke is associated with the use of the drug in this population. On the same day, the European Medicines Agency (EMEA) announced that after its review of the same data, the EMEA's Committee for Medicinal Products for Human Use had recommended that the marketing of sibutramine be suspended in the European Union.

Until now, the sibutramine label had included a warning against its use in patients with cardiovascular disease, but "based on the serious nature of the review findings, FDA requested and the manufacturer agreed to add a new contraindication," according to the agency's statement. The FDA is advising that clinicians regularly monitor the blood pressure and heart rate of their patients on sibutramine, and "if sustained increases in blood pressure and/or heart rate are observed, sibutramine should be discontinued."

The advisory adds that sibutramine should be discontinued in patients who do not lose at least 5% of their baseline body weight within the first 3-6 months of treatment, "as continued treatment is unlikely to be effective and exposes the patient to unnecessary risk."

Sibutramine, a serotonin-norepinephrine reuptake inhibitor marketed as Meridia by Abbott Laboratories, was approved in 1997.

Concerns about increases in blood pressure and heart rate associated with sibutramine date back to a 1996, when an FDA advisory panel agreed the drug was effective in trials, but voted 5-4 against approval, based largely on concerns over increases in mean blood pressure and heart rate over placebo at all doses studied.

The new contraindication states that sibutramine "is not to be used in patients with a history of cardiovascular disease," including history of coronary artery disease, history of stroke or transient ischemic attack, history of heart arrhythmias, history of heart failure, history of peripheral arterial disease, and uncontrolled hypertension (such as over 145/90 mm Hg).

The data reviewed by the FDA and EMEA were from the Sibutramine Cardiovascular Morbidity/Mortality Outcomes in Overweight or Obese Subjects at Risk of a Cardiovascular Event (SCOUT) study, which compared placebo plus standard care to sibutramine and standard care in about 10,000 overweight or obese patients aged at least 55 years, with a history of cardiovascular disease (CVD) or type 2 diabetes and one additional cardiovascular risk factor.

The study was designed to show that weight loss with sibutramine was more effective in lowering the number of cardiovascular events than with placebo, according to the FDA. But the rate of cardiovascular events among those on sibutramine was 11.4%, compared with 10% in placebo patients, according to preliminary data reported by the FDA in November 2009.

Further review of the data showed that only those participants who had a history of CVD were at an increased risk for cardiovascular events, according to the Jan. 21 statement. Among those with a history of CVD only, and not diabetes, the event rate was 8.3% in those taking placebo, compared with 10.1% in those on sibutramine, a nonsignificant difference.

The difference in cardiovascular event rates between groups did reach statistical significance in patients with both CVD and diabetes, at 11.9% in placebo patients vs. 13.9% in those taking sibutramine. But in patients with diabetes and no history of CVD, the event rates were identical, at 6.5%.

The FDA is planning to hold another advisory panel meeting to discuss the risk-benefit profile of sibutramine and whether any further regulatory action is needed to ensure the safe use of the drug, the statement said. ■