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IN BRIEF

Tegaserod *(Zelnorm)* Returns

Tegaserod maleate *(Zelnorm)*, a 5-HT_4 receptor partial agonist that increases gastrointestinal (GI) motility, was approved by the FDA in 2002 for short-term treatment of irritable bowel syndrome with constipation (IBS-C) in women and in 2004 for treatment of chronic idiopathic constipation (CIC) in adults <65 years old.

In 2007, the manufacturer (Novartis) complied with an FDA request to stop marketing the drug based on an unpublished retrospective analysis of clinical trials in IBS-C and other GI motility disorders that showed a higher rate of ischemic cardiovascular events (including cardiovascular death, nonfatal myocardial infarction [MI], and nonfatal stroke) in patients who took tegaserod than in those who took placebo. Among more than 11,600 patients treated with tegaserod for 1-3 months, 13 (0.11%) had a confirmed ischemic event compared to only 1 (0.01%) of more than 7000 patients who received placebo.[1]

The mechanism by which tegaserod could cause cardiovascular ischemia is unknown; 5-HT_1 receptor agonists used to treat migraine, such as sumatriptan (*Imitrex*, and others), can constrict coronary arteries, and tegaserod has some affinity for 5-HT_1 receptors.[1]

Based on a re-examination of the data that led to withdrawal of tegaserod and the continued need for a drug with this mechanism of action to treat IBS-C, an FDA advisory committee recommended approval of a supplemental new drug application from a new sponsor (Sloan). The drug is now approved only for treatment of IBS-C in women <65 years old and is contraindicated in patients with a history of MI, stroke, transient ischemic attack, or angina.

Prucalopride *(Motegrity)*, a selective 5-HT_4 receptor agonist recently approved by the FDA for treatment of CIC, will be reviewed in a future issue. It has less affinity for 5-HT_1 receptors than tegaserod.[2] ■

1. In brief: tegaserod withdrawn. Med Lett Drugs Ther 2007; 49:40.
2. J Tack et al. Systematic review: cardiovascular safety profile of 5-HT_4 agonists developed for gastrointestinal disorders. Aliment Pharmacol Ther 2012; 35:745.

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