FDA Cardiology Drugs Panel Backs Prasugrel

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SILVER SPRING, MD. — A Food and Drug Administration advisory panel voted unanimously to recommend that the antiplatelet drug prasugrel be approved for treating patients with acute coronary syndrome, who present with unstable angina, non–ST-segment elevation myocardial infarction, or ST elevation MI.

At a meeting this month, all nine voting members of the FDA's Cardiovascular and Renal Drugs Advisory Committee agreed that prasugrel—a drug that was shown to be more effective than clopidogrel in preventing cardiovascular events, but with a higher rate of serious bleeding in a study of more than 13,000 patients with acute coronary syndromes (ACS)—had a favorable benefit-to-risk profile.

Prasugrel is a thienopyridine, developed by Eli Lilly & Co. and Daiichi Sankyo Inc., which have proposed that it be approved for reducing cardiovascular

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events in patients with ACS, with unstable angina (UA) or non–ST-segment elevation myocardial infarction (NSTEMI), when managed with PCI, and patients with STEMI when managed with primary or delayed percutaneous coronary intervention (PCI).

Prasugrel, administered as a 60-mg loading dose followed by 10 mg/day, was compared with clopidogrel, administered at a 300-mg loading dose followed by 75 mg/day, in the Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel-Thrombolysis in Myocardial Infarction (TRITON-TIMI 38), an international double-blind study of 13,608 patients with moderate to high-risk ACS, scheduled to have PCI. They had UA, NSTEMI, or STEMI. All patients were on aspirin.

Over a mean of 12 months, the primary end point, a composite of cardiovascular death, MI, or nonfatal stroke, occurred in 12.1% of the clopidogrel group, compared with 9.9% of the patients taking prasugrel, a significant reduction. Broken down by severity of presentation, the occurrence of the primary end point in the non-STEMI/UA group was 12% among those on clopidogrel, compared with 9.9% among those on prasugrel, a statistically significant difference. The rate in the STEMI group was 12.4% in those on clopidogrel, compared with 10.0% in those on prasugrel, also a significant difference.

The rate of strokes in both groups was 0.9%; the overall risk of cardiovascular death was also not significantly different between the two groups.

The main risk was bleeding. The rate of major bleeding was 2.2% in those on prasugrel, compared with 1.7% in those on clopidogrel; the rates of life-threatening bleeding, including fatalities, were 1.3% and 0.8%, respectively; fatal bleeding occurred in 0.3% a 0.1%; and intracranial hemorrhage rates were 0.3% and 0.2%. Bleeding most often occurred around the time of PCI, and was much higher after a coronary artery bypass graft (CABG).

The FDA's analysis of the overall risk-benefit profile of the drug showed that for every 1,000 patients with ACS treated with prasugrel, the treatment prevents 21 nonfatal MIs, three cardiovascular deaths, with no strokes, but at a cost of two fatal hemorrhages, three nonfatal major hemorrhages, five minor hemorrhages, and 19 minimal hemorrhages.

All panelists agreed that labeling should discourage physicians from prescribing prasugrel to treat patients with a history of stroke or TIA. Among patients over age 70 years, bleeding was not more common with prasugrel, but the sequelae were more serious.

The FDA usually follows the recommendations of its advisory committee. If approved, prasugrel will be marketed as Effient. Upon its approval, the company is ready to launch immediately, a company official said after the meeting. ■