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Blood Thinner's Approval A Muted Win For Lilly

Matthew Herper, 07.10.09, 6:40 PM ET

The Food and Drug Administration has approved Effient, a blood thinner made by Daiichi Sankyo and Eli Lilly, after an 18-month delay.

But Effient will carry stark "black box" warnings about the risk of deadly bleeding. Such warnings are not borne by Effient's main competitor, Plavix.

That could make it difficult for Effient to capture market share from Plavix, which generates $6 billion a year in sales for makers Sanofi-Aventis and Bristol-Myers Squibb and is the second-biggest selling drug in the world. Effient is only approved for patients who have undergone angioplasty surgery to unclog a blocked artery; this is a fraction of the Plavix market. The U.S. patent on Plavix will expire in three years, potentially flooding the market with cheap generics.

The warning says: "Effient can cause significant, sometimes fatal bleeding." It tells doctors not to prescribe the drug in patients with "pathological bleeding" or in those with a history of strokes or mini-strokes. It also says that Effient is "not recommended" in patients older than 75 years of age unless they are especially at risk of heart disease, and states underweight people and those on certain medicines are at increased risk for serious bleeding.

"We think being able to get this approved and available will be an important option for the patients who have acute coronary syndrome and are being treated with [angioplasty]," says Anthony Ware, the Lilly executive who directed Effient's development. He says the company has "never shied away" from the drug's bleeding risks.

In a victory for Lilly, a lower, half-dose of the pill was approved, even though it was not tested in the main clinical trials for Effient. That may lead doctors to use the drug in patients who would otherwise have a higher bleeding risk, such as the underweight.

The difficulty of evaluating the drug is that while it reduced the number of non-fatal heart attacks, compared with Plavix, it also increased the rate of dangerous bleeding, says Robert Temple, director of the FDA's office of drug evaluation. In a 13,608-patient clinical trial, 7% of those taking Effient had heart attacks, compared with 9.1% of those taking Plavix, but it did not decrease the overall number of deaths.

Effient, known by the generic name prasugrel, traipsed a tortured, delayed path through the FDA. At an advisory panel meant to evaluate the drug, one critic, Sanjay Kaul of Cedar-Sinai Medical Center, was excluded at the last minute after originally being named as a voting member of the panel.

Kaul says that the warning is "sufficient" but that he would like to be clearer that Effient's benefits over Plavix are driven mainly by differences in heart attacks, not by differences in overall death or stroke.

Two doctors said they expect interventional cardiologists, who perform angioplasty procedures, to use Effient often, but think it is unlikely that the drug will be used outside of this narrow indication.

"I think the interventionalists love it, but others are going to look at the drug and try to figure out what to do with it," says Howard Weintraub, clinical director at NYU Center for the Prevention of Cardiovascular Disease.

"I do not see Effient supplanting Plavix for most patients," says William Boden, a professor at the University of Buffalo. "Plavix has been around for almost 10 years, is effective in most patients, and is largely safe with an acceptable bleeding profile."

One group Effient could benefit, Boden says, are "frequent fliers" who keep returning with new heart attacks or bad chest pain--potentially because their Plavix isn't working for genetic or other reasons.

Effient does not seem to have this same problem, which may explain some of its increased efficacy. In a large study comparing Effient and Plavix in a much broader patient population, Eli Lilly and Sankyo are collecting this genetic data. Temple, the FDA officials, says he hopes this will help in determining who should get which drug.