FDA Panel: Ortho Evra Benefits Outweigh Risks

BY ELIZABETH MECHCATIE

FROM A MEETING OF THE FDA'S REPRODUCTIVE HEALTH DRUGS ADVISORY COMMITTEE AND THE DRUG SAFETY AND RISK MANAGEMENT ADVISORY COMMITTEE

ADELPHI, MD. – Advisors to the Food and Drug Administration voted 19-5 that the benefits of the Ortho Evra contraceptive patch outweighed its risks, although they agreed with epidemiologic evidence that use of the patch is associated with an increased risk of venous thromboembolic events.

At a joint meeting of the FDA's Reproductive Health Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee, panelists agreed that the risk of venous thromboembolic events (VTEs) associated with the Ortho Evra patch was greater than the VTE risk associated with combination oral contraceptives (COCs) that contain 35 mcg or less of ethinyl estradiol. But those who agreed that Ortho Evra had a favorable risk-benefit profile cited the unique features that the patch provides women, since it is the only transdermal contraceptive available in the United States and is an alternative to having to take a daily pill, and that it was important for women to have a range of contraceptive options available. Several of the panelists who voted positively on the risk-benefit question said they would have voted no if the product had been a pill.

The panel also voted 20-3, with 1 abstention, that information about the risk-benefit profile of Ortho Evra in the prescriber and patient labels should be improved, and recommended revisions to the labels to reflect the available risk-benefit data, including the results of an FDA-funded study that found the risk of VTEs was increased in Ortho Evra users.

Ortho Evra was approved in November 2001 and contains 6 mg of norelgestromin and 750 mcg of ethinyl estradiol in a patch that is worn for 3 weeks, followed by 1 patch-free week. Exposure to ethinyl estradiol with the patch is about 60% higher than a COC containing 35 mcg of ethinyl estradiol.

Postmarketing reports of thrombotic and thromboembolic events associated with Ortho Evra appeared to be higher than rates with some COCs, so the manufacturer, Janssen Research and Development LLC, initiated two epidemiologic studies using insurance claims databases in 2005. One found the risk of VTEs was about twofold higher in women on Ortho Evra, compared with those on a COC containing norgestimate and 35 mcg of ethinyl estradiol. The other study found no increased VTE risk.

Earlier this year, a boxed warning was added to the Ortho Evra label that advises clinicians to balance the higher estrogen exposure with the patch and the "possible increased risk of VTE with the patch, against the chance of pregnancy."

The FDA position is that there is no clear answer as to whether Ortho Evra is associated with an increased risk of VTE, compared with COCs, and that none of the studies to date provide a definite answer about the relative risk of thrombotic and thromboembolic events with Ortho Evra. The FDA-funded study, reported in October 2011, using insurance claims databases, found that use of Ortho Evra was associated with about a 50% increased risk of VTEs, compared with low-dose combined hormonal contraceptives.

The consumer representative on the panel, Michele Orza, Sc.D., principal policy analyst at the National Health Policy Forum at George Washington University, Washington, said she voted yes on the risk-benefit question, "with great difficulty." In the case of Ortho Evra, she said, "I think there is additional risk related to second-generation oral contraceptives, but it is a unique kind of a product … and I thought it was important to preserve that option."

However, Dr. Orza added that the Ortho Evra patch is associated with a "nontrivial" increase in VTE risk, "so it needs to be prescribed very carefully and with a lot of knowledge on the part of both the clinician and patient," with a discussion about how this risk compares to the risk with other contraceptive options.

Panelists have been cleared of potential conflicts of interest related to the topic of the meeting. Occasionally, a panelist may be given a waiver, but not at this meeting. ■