

Emerging Data Link Psoriasis to Comorbidities

BY DOUG BRUNK
San Diego Bureau

SAN DIEGO — Emerging scientific data on adults with psoriasis suggest that certain comorbidities, including metabolic syndrome and myocardial infarction, may accompany the disease.

People with psoriasis “have a tendency to be obese, have a higher rate of cardiovascular disease [and] higher rates of stroke over time; they tend to smoke more, and they have a higher prevalence of depression,” Dr. Lawrence F. Eichenfield said at a meeting on skin disorders sponsored by Rady Children’s Hospital. “One [question] that needs to be addressed is, are those secondary factors because they have psoriasis and they feel depressed,



For severe psoriasis, phototherapy is preferred. The relative risk-benefit is reasonable.

DR. EICHENFIELD

and they’re starting to eat and they get obese and have secondary cardiovascular effects? Or is it something about the psoriasis itself, something that is going along with inflammatory disease?”

One study found that 20- to 30-year-olds with severe psoriasis had a 310% increased risk of having a myocardial infarction, compared with age-matched controls who did not have the disease (JAMA 2006;296:1735-41).

“So in adults, the younger you are, the relatively higher risk you have,” said Dr. Eichenfield, chief of pediatric and adolescent dermatology at Rady Children’s Hospital, San Diego.

At present, however, the effect of psoriasis treatment on the risk of myocardial infarction or on other comorbidities is unknown.

Also unknown is how these emerging findings in adults can be translated into pediatric and adolescent patients with psoriasis. “There is a real paucity of data,” said Dr. Eichenfield, who is also a professor of pediatrics and medicine at the University of California, San Diego. “In one prospectively designed study, we tested etanercept for psoriasis in children and adolescents. Clearly, there was a higher body mass index in that population compared with controls. The real question is, how much is the inflammatory component of psoriasis contributing to this?”

In adults, the prevalence of psoriasis is estimated to be 2.2%, he said. Of those, 25% have moderate to severe disease.

Data in children and adolescents vary, but the prevalence of psoriasis in that population ranges from 0.55% to 1.0%. There are no good prospective pediatric data, he said. “If you ask adults when their psoriasis began, about one-third of them say it began during childhood or adolescence.”

Plaque psoriasis, affecting up to 84% of cases, is the most common presentation in pediatric patients. “It’s certainly the type

of psoriasis that causes more trouble,” Dr. Eichenfield said. “Face and intertriginous areas are commonly affected in children, so many times we’ll have individuals who present with scalp psoriasis, and then over a long period of time we start seeing more typical cutaneous plaques on the elbows, knees, and buttocks.”

Two medium- and low-potency topical therapies are approved for short-term use in pediatric psoriasis: mometasone furoate and alclometasone dipropionate.

Other topical therapies that are being used include other corticosteroids; topical calcipotriol; tars and anthracyclines; tazarotene; and topical calcineurin inhibitors.

For severe psoriasis, phototherapy is Dr. Eichenfield’s intervention of choice “in terms of the relative risk-benefit” ratio, he said. “It seems reasonable.”

Other unapproved treatments currently being used in pediatric psoriasis include immunosuppressive agents, systemic retinoids,

and biologic agents, all of which carry a significant risk of side effects and toxicities.

Dr. Eichenfield disclosed that he has received grant and research support from Amgen Inc., Galderma Laboratories LP, Obagi Medical Products Inc., and Johnson & Johnson. He has also received honoraria from Medicis Pharmaceutical Corp. and Ranbaxy Pharmaceuticals Inc., and serves as a consultant to Amgen, Galderma, Obagi, Medicis, and Stiefel Laboratories Inc. ■

IMPORTANT CORRECTION OF DRUG INFORMATION ABOUT EFFEXOR XR® (VENLAFAXINE HCl) EXTENDED-RELEASE CAPSULES

An advertisement in professional journal publications for EFFEXOR XR® (venlafaxine HCl) Extended-Release Capsules for the treatment of major depressive disorder was the subject of a Warning Letter issued by the U.S. Food and Drug Administration (FDA) in December 2007. The FDA stated that the journal ad was misleading because it overstated the efficacy of EFFEXOR XR, made unsubstantiated superiority claims, and contained other unsubstantiated claims regarding EFFEXOR XR.

Wyeth would like to take this opportunity to clarify the content of the advertisement.

Claims that Reference the Baldomero et al Study and Other Related Claims

The FDA objected to the claim, “In an open-label study of patients who failed previous antidepressant treatment, nearly 60% achieved remission when changed to EFFEXOR XR.” The FDA determined that the Baldomero study (the cited reference for this claim) could not be relied upon as substantial evidence to support the claim due to the following reasons: (1) the study was an open-label study, which is not an appropriate study design to measure subjective end points because it fails to minimize potential bias; (2) the study did not include a placebo group, so there was no way to determine the actual effect size of the drug; and (3) the study did not provide information about whether EFFEXOR XR was superior to failed therapy because study subjects were not randomized to their previously failed therapy. Therefore, the FDA stated that the study failed to support the 60% remission rate claim as well as any conclusion that EFFEXOR XR is superior to other antidepressant treatments. In addition to the above claim, the FDA stated that other claims added to the misleading impression that patients who have failed previous antidepressant therapy can expect improvement when switching to EFFEXOR XR.

Claims from the PREVENT Study

The FDA objected to the claim, “In the PREVENT study, the probability of preventing a new episode of depression was 92% with EFFEXOR XR in maintenance year 2 vs. 55% with placebo.” The FDA stated that the cited claim overstated the efficacy of EFFEXOR XR by implying that the general patient population suffering from major depressive disorder can expect a 92% probability of preventing a recurrent depressive episode after two years of treatment when this is not supported by substantial evidence.

The cited study for this claim was a randomized, multicenter, double-blind study (n=1096) comparing EFFEXOR XR with placebo. The study was designed to provide efficacy data regarding recurrence prevention with EFFEXOR XR after two years of maintenance

treatment. It followed patients through 4 different time periods: a 10-week acute period, a 6-month continuation period, an initial 12-month maintenance period (maintenance year 1), and a second 12-month maintenance period (maintenance year 2). At the end of each period, patients were only considered eligible for inclusion in the next period if they were still responding to the drug. Patients dropped out of the study during each of the periods for different reasons (eg, lack of efficacy, adverse events). At the start of each maintenance period, the remaining patients who still showed a response to EFFEXOR XR were re-randomized to EFFEXOR XR or placebo. Because a high percentage of EFFEXOR XR patients were either re-randomized to placebo or were discontinued from the study before entering maintenance year 2 and because only patients who responded to EFFEXOR XR were selected to continue to the next phase of treatment, the FDA determined that the results of the study could not be extrapolated to the general patient population suffering from major depressive disorder.

Claim Regarding Clinical Experience and Number of Patients

The FDA objected to the claim, “More than 12 years of clinical experience and over 20 million patients treated with EFFEXOR/EFFEXOR XR.” The claim of 20 million EFFEXOR/EFFEXOR XR patients was estimated from the number of U.S. prescriptions, average daily consumption, and average length of therapy. The FDA determined that this claim was misleading based on the referenced data because the calculations used did not reflect the number of “unique” patients. Because there are no unique patient-level data available for the entire 14-year period during which EFFEXOR/EFFEXOR XR has been on the U.S. market, the claim is no longer used in EFFEXOR XR promotional materials.

Please see brief summary of Prescribing Information on adjacent page.

EFFEXOR® and EFFEXOR XR® are registered trademarks of Wyeth Pharmaceuticals Inc.

Wyeth® © 2008, Wyeth Pharmaceuticals Inc., Philadelphia, PA 19101 236624-01 July 2008