

## CORRESPONDENCE



## Cardiovascular Toxicity of Valdecoxib

**TO THE EDITOR:** Rofecoxib (Vioxx) was recently withdrawn from the market because of an increased risk of myocardial infarction and stroke. There is a similar public health concern about another coxib, valdecoxib (Bextra), which is used by 7 million patients worldwide.<sup>1</sup> To protect the safety of the public, we write to recommend that clinicians stop prescribing valdecoxib except in extraordinary circumstances. This recommendation is based on the long delay between the initial evidence of the cardiotoxicity of rofecoxib and its withdrawal, recent studies demonstrating the cardiotoxicity of valdecoxib in high-risk patients, the availability of other therapies not currently known to have cardiovascular risks, and the lack of compelling evidence of countervailing benefits. We believe this restriction should remain in effect until there are better safety data for valdecoxib.

Two randomized, placebo-controlled clinical trials in patients immediately after coronary-artery bypass grafting showed that valdecoxib increased the risk of serious cardiovascular outcomes by a factor of approximately three.<sup>2</sup> Pfizer, the manufacturer, acknowledged the cardiotoxicity and agrees that “the company cannot ethically test Bextra in patients at high risk for heart disease.”<sup>3</sup> The crucial public health question concerns the safety of patients who are taking lower doses of valdecoxib for musculoskeletal disorders, most of whom have a lower baseline risk of cardiovascular events. There are inadequate data on the cardiovascular safety of valdecoxib in this population, but given the strong signal from the bypass studies, it is prudent to limit the use of valdecoxib until there are convincing data supporting its cardiovascular safety.

The label for valdecoxib was revised in November 2004 by the manufacturer to include a black-box warning regarding serious skin reactions and a contraindication for use in patients who have un-

dergone bypass surgery. These changes to the label do not address concerns about the cardiovascular safety of the drug in the general population. Even for patients with cardiovascular disease, experience has shown that label changes have little, if any, effect on prescribing. The manufacturer is planning a multiyear trial.<sup>3</sup> Meanwhile, millions of patients will continue to take valdecoxib.

We believe the doubts raised about the safety of valdecoxib constitute a potential imminent hazard to public health and thus require action.

Wayne A. Ray, Ph.D.  
Marie R. Griffin, M.D., M.P.H.  
C. Michael Stein, M.B., Ch.B.

Vanderbilt University School of Medicine  
Nashville, TN 37232

Dr. Ray reports having received consulting fees and research support from Pfizer, and Dr. Griffin research support from Pfizer and consulting fees from Merck.

1. Winslow R. Researcher raises flag on painkiller. *Wall Street Journal*. November 11, 2004:D6.
2. BEXTRA: valdecoxib tablets. (Accessed December 4, 2004, at [http://www.pfizer.com/download/uspi\\_bextra.pdf](http://www.pfizer.com/download/uspi_bextra.pdf).)
3. Harris G. Shades of the Vioxx case for another drug. *New York Times*. November 21, 2004(Section 4):3.

### THIS WEEK'S LETTERS

- 2767 **Cardiovascular Toxicity of Valdecoxib**
- 2768 **Oral Dexamethasone for Mild Croup**
- 2770 **Management of Cutaneous Melanoma**
- 2771 **Case 25-2004: A Woman with Severe Obesity, Diabetes, and Hypertension**
- 2773 **ER- $\beta$  in Prostate Cancer**
- 2774 **Blinding Endophthalmitis from Orthodontic Headgear**