Vioxx, We Hardly Knew Ya

By ACSH Staff — October 18, 2004

The recent withdrawal of Merck’s blockbuster COX-2 inhibitor, the anti-arthritis pain reliever Vioxx (rofecoxib), was a major blow to a number of interested parties. Merck, of course, took the biggest hit. But the millions of arthritis sufferers who depended on reliable and safe relief from pain since Vioxx’s approval in 1999 are also confused and upset, and the federal drug regulators at the FDA are in the midst of a losing streak of unprecedented proportions.

The FDA folks have come under increasing attack over the past few months. The demand for allowing re-importation of cheaper drugs from Canada has attained fever pitch, which the FDA has thus far resisted. Next came the controversy over the safety of anti-depressants prescribed for children, with some accusing the FDA of suppressing their own expert’s comments. Then the recent loss of half of America’s flu vaccine due to sterility breakdowns at the American-owned Chiron facility in Liverpool was alleged to have been due, in part, to a failure of adequate FDA oversight -- our Centers for Disease Control (CDC) have been forced to go scrounging the world for spare vaccine to protect our vulnerable elderly and infirm.

Now we have the Vioxx withdrawal, precipitated by Merck’s own multi-year study, designed not to assess cardiovascular risk, but to determine if the drug prevents the onset of colon polyps in susceptible patients. This study showed evidence of an almost doubled risk of heart events or strokes after eighteen months of therapy. Merck made the tough decision to voluntarily withdraw the drug worldwide, at least partially in fear of a torrent of liability lawsuits predicated on the alleged adverse heart effects. Another reason, as stated by Merck, was the continued availability of alternative COX-2 drugs. It seems likely that if Vioxx were the only member of its class, some course of action short of complete withdrawal would have been deemed appropriate -- such as a "black-box" warning to physicians to avoid using it in patients with possibly elevated heart risk.

Predictably, so-called "consumer" groups with 20/20 hindsight have taken out their trusty retrospectoscopes -- the only medical instrument guaranteed 100% accurate -- and condemned the FDA for not banning Vioxx three years ago, when a preliminary study indicated a possible increase in cardiovascular risk among patients taking the drug. Congressional investigations are being called for to look into an allegedly incestuous (or at least conspiratorial) relationship between Merck and the good ole boys at the FDA -- the pharmaceutical industry and the FDA being the latest favorite whipping boys of the political set.

But these critics neglected to take into account the fact that Vioxx, like the other COX-2 drugs (Pfizer’s Celebrex and Bextra), was prescribed specifically to alleviate arthritis pain while posing less danger to the stomach and GI tract. The older anti-arthritis drugs, known as NSAIDs, are notorious for irritating the gut, sometimes causing bleeding severe enough to require hospitalization. Among all classes of drugs, these were among the most common causes of
serious adverse drug reactions. Some estimates attribute over 10,000 deaths annually to NSAID complications. How many such complications have been prevented by the use of Vioxx instead of one of the older NSAIDs? No one can be sure, but the number is substantial. I practiced rheumatology for twenty years and had to care for many patients suffering the ill effects of NSAIDs -- there was no COX-2 option at that time.

Another valuable lesson gleaned from the Vioxx episode is the benefit to consumers of "me-too" drugs, whose production and marketing has been condemned in recent attacks on the pharmaceutical industry. No matter how similar drugs may be in chemical structure, some patients will respond to one and not another, while some will exhibit intolerance to one and not another. Indeed, Merck itself hopes to launch another COX-2 inhibitor within the next few months.

Some editorials went so far as to call for restrictions on the other COX-2 drugs, based on data from the Merck-Vioxx study alone. Yet there is no solid evidence incriminating the others in cardiovascular risk, only suspicion. While those patients now on Celebrex and Bextra are concerned about the potential risks, more studies should be done evaluating these risks before restrictions are added. This remains true despite the recent news about the possible link between Bextra -- given intravenously -- and increased heart risk among bypass patients in a small study.

No other anti-arthritis drugs, including aspirin and the older NSAIDs, have been studied over the length of time that Vioxx has been. Even aspirin would not be approved for human use if it had to pass FDA evaluation today, due to its propensity for inducing GI bleeding, allergic reactions, and blood thinning. Indeed, while critics accuse the FDA of being lax, the opposite is true: getting an innovative, life-saving pharmaceutical to market in the U.S. is an incredibly daunting, time-consuming, and expensive endeavor.

The withdrawal of Vioxx may also mean that our progress toward reducing the toll of colorectal cancer will be slowed. The results of the new Merck-Vioxx study will soon be made public, but preliminary word indicates that significant benefit in reducing the occurrence of pre-malignant colon polyps was demonstrated.

What now will be the fate of this important drug? Hopefully, with appropriate cautions, it can be resurrected as a chemopreventive agent against colorectal cancer. Someday, it may again find a niche in the form of selected arthritis sufferers with low cardiovascular risk.

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