

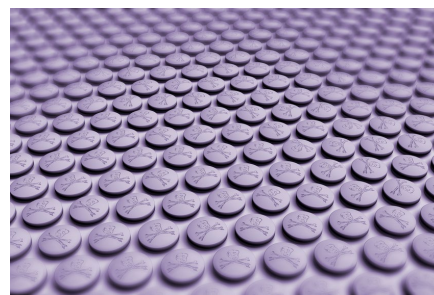
Amanda's Absence: Should Vioxx Be Kept Off the Market?

by

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Part I—Withdrawals

“Amanda missed bio lab again this week.”

This was not what Dr. Sharpe had expected to hear when his teaching assistant knocked on his door late one Tuesday afternoon in March. Amanda was an exceptional student. She had been born with Type III osteogenesis imperfecta, a painful and debilitating condition in which bones break and deform easily. Despite her condition, Amanda had earned top academic honors during high school and came to college on a merit scholarship. Before a month ago, she had never missed a single lecture or lab, but thinking back, Dr. Sharpe could not remember her attending his class for at least a week. Was there something seriously wrong?

The Student Health Center had no information, but a phone call to Dr. Rutter, the Dean of Students, cleared up the mystery. “Amanda has asked to withdraw for this semester for medical reasons. It seems she can’t control her pain anymore, now that Vioxx is off the market.”

Dr. Sharpe remembered the Food and Drug Administration had announced that two pharmaceutical companies were withdrawing Vioxx and Bextra from the market because they caused heart attacks. Both were in the same drug class, the Cox-2 inhibitors. He also vaguely remembered commercials pitching Vioxx to senior citizens for arthritis pain.

Questions

1. Some prescription drugs may remain on the market 20 years or more. Others are removed shortly after being introduced. Give three to four reasons that a drug might be removed from the market, either by the FDA or its maker. Is every reason true for every drug?
2. How might the manufacturers have determined that Vioxx increases the risk of heart attack? Based on your answers, when would they have learned this information?
3. What other facts or information might Dr. Sharpe (or you) want to know about Vioxx? About Amanda’s condition?



Part II—Press Release

Dr. Sharpe was stunned to hear that Amanda would be forced to leave school just because one medication was not available. He went to the Food and Drug Administration's web site, where he found their initial press announcement.

Sept. 30, 2004*

FDA Issues Public Health Advisory on Vioxx; Manufacturer Voluntarily Withdraws Product

The Food and Drug Administration (FDA) today acknowledged the voluntary withdrawal from the market of Vioxx (chemical name rofecoxib), a non-steroidal anti-inflammatory drug (NSAID) manufactured by Merck & Co. FDA today also issued a Public Health Advisory to inform patients of this action and to advise them to consult with a physician about alternative medications.

Merck is withdrawing Vioxx from the market after the data safety monitoring board overseeing a long-term study of the drug recommended that the study be halted because of an increased risk of serious cardiovascular events, including heart attacks and strokes, among study patients taking Vioxx compared to patients receiving placebo. The study was being done in patients at risk of developing recurrent colon polyps.

“Merck did the right thing by promptly reporting these findings to FDA and voluntarily withdrawing the product,” said Acting FDA Commissioner Dr. Lester M. Crawford. “The risk that an individual patient would have a heart attack or stroke is very small. Yet their study does suggest patients taking Vioxx chronically face twice the risk of a heart attack compared to patients receiving a placebo.”

In June 2000, Merck had submitted to FDA a separate safety study that showed an increased risk of heart attacks and strokes in patients taking Vioxx chronically for arthritis, compared to patients taking Aleve. After reviewing the results of the earlier study, FDA required additional label and prescribing information on Vioxx, but did not recommend withdrawal.

FDA approved Vioxx in 1999 for the reduction of pain and inflammation caused by osteoarthritis, rheumatoid arthritis, and acute pain in adults. It is a Cox-2 selective NSAID; other NSAIDs target both Cox-1 and -2. When Vioxx was approved, it was hoped that it would have a lower incidence of gastrointestinal ulcers and bleeding than other NSAIDs like Motrin (ibuprofen) and Aleve (naproxyn).

**Based on the original FDA press release, which has been modified for the purposes of this case study.*

Questions

1. What are the advantages and disadvantages of Vioxx versus other pain-relieving medicines? Why are these important?
2. According to the data provided to FDA, are all patients taking Vioxx at greater risk of a heart attack or stroke? Why or why not?
3. What are two other questions that you have about the Vioxx withdrawal that were not addressed by the press release?



Part III—Prepared Testimony

The more he read, the more Dr. Sharpe realized that the Vioxx withdrawal was a major event. The FDA had posted pages of reports, press briefings, and letters to physicians and the public. There even was a formal hearing before the Senate Committee on Finance on the matter. He read the opening statements from the testimony of Sandra Kweder, M.D., Deputy Director of the Office of New Drugs, given on November 18, 2004.*

“Members of the Committee, we appreciate this opportunity to discuss drug safety and the worldwide withdrawal by Merck & Co. of Vioxx. Modern drugs provide significant health benefits. We believe FDA maintains the highest worldwide standards for drug approval.

All drugs pose some level of risk. Unless a new drug’s demonstrated benefits outweigh its known risks for the intended population, FDA will not approve the drug. FDA only grants approval once a sponsor demonstrates through clinical trials that a drug is safe and effective. However, our experience has shown we cannot anticipate all adverse effects of a drug before approval, because not every adverse drug reaction occurs during pre-approval trials.

Occasionally, serious adverse effects are identified after approval, in post-marketing clinical trials or through spontaneous reporting of adverse events. Adverse effects also result from errors in drug prescribing, dispensing or use. FDA has a strong post-market drug safety program designed to uncover adverse events that happen after initial approval. Drug safety staff evaluate and respond to adverse events identified by ongoing clinical trials, or as reported by physicians or patients. Our recent actions concerning the drug Vioxx illustrate the importance of continuing to assess the safety of a product once it is in widespread use.

Detecting and limiting adverse reactions can be challenging. How do we weigh the impact of adverse drug reactions against the benefits of a product to individual patients and the public health? The question is multifaceted and complex, involving scientific as well as public policy issues.”

**Based on the original testimony, which has been modified for the purposes of this case study.*

Questions

1. What are two strengths and two weaknesses in the current system of drug approval? Why did you choose these particular strengths and weaknesses?
2. Based on your answers to Question 1 above, did the FDA approve Vioxx too soon? Why or why not? Could the approval system be changed in a way that prevented the heart attack deaths attributed to Vioxx?
3. Should Merck & Co. be punished for putting an unsafe drug on the market? Why or why not?



Part IV—Review Panel

Merck & Co. has petitioned the FDA for permission to return Vioxx to the market, with additional warning labels and dispensing information. Both you and Dr. Sharpe have been appointed to a review panel that must make a written recommendation to the Assistant Director of FDA, either for or against allowing Vioxx back on the market. What would you recommend, and why?

In crafting your response, you may discuss the general issues with other staff members (members of your work group or class), and you are free to include research findings or data from outside primary resources. However, you must write your own individual recommendation and clearly explain the rationale for your recommendation. Your recommendation and rationale for it is limited to one typed page.

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