

FDA News

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FDA

FDA Issues Public Health Advisory on Vioxx as its Manufacturer Voluntarily Withdraws the 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 from the market," said Acting FDA Commissioner Dr. Lester M. Crawford. "Although the risk that an individual patient would have a heart attack or stroke related to Vioxx is very small, the study that was halted suggests that, overall, patients taking the drug chronically face twice the risk of a heart attack compared to patients receiving a placebo."

Dr. Crawford added that FDA will closely monitor other drugs in this class for similar side effects. "All of the NSAID drugs have risks when taken chronically, especially of gastrointestinal bleeding, but also liver and kidney toxicity. They should only be used continuously under the supervision of a physician."

FDA approved Vioxx in 1999 for the reduction of pain and inflammation caused by osteoarthritis, as well as for acute pain in adults and for the treatment of menstrual pain. It was the second of a new kind of NSAID (Cox-2 selective) approved by FDA. Subsequently, FDA approved Vioxx to treat the signs and symptoms of rheumatoid arthritis in adults and children.

At the time that Vioxx and other Cox-2 selective NSAIDs were approved, it was hoped that they would have a lower risk of gastrointestinal ulcers and bleeding than other NSAIDs (such as ibuprofen and naproxen). Vioxx is the only NSAID demonstrated to have a lower rate of these side effects.

Merck contacted FDA on September 27, 2004, to request a meeting and to advise the agency that the long-term study of Vioxx in patients at increased risk of colon polyps had been halted. Merck and FDA officials met the next day, September 28, and during that meeting the company informed FDA of its decision to remove Vioxx from the market voluntarily.

In June 2000, Merck submitted to FDA a safety study called VIGOR (Vioxx Gastrointestinal Outcomes Research) that found an increased risk of serious cardiovascular events, including heart attacks and strokes, in patients taking Vioxx compared to patients taking naproxen. After reviewing the results of the VIGOR study and other available data from controlled clinical trials, FDA consulted with its Arthritis Advisory Committee in February 2001 regarding the clinical interpretation of this new safety information. In April 2002, FDA implemented labeling changes to

reflect the findings from the VIGOR study. The labeling changes included information about the increase in risk of cardiovascular events, including heart attack and stroke.

Recently other studies in patients taking Vioxx have also suggested an increased risk of cardiovascular events. FDA was in the process of carefully reviewing these results, to determine whether further labeling changes were warranted, when Merck informed the agency of the results of the new trial and its decision to withdraw Vioxx from the market.

Additional information about this withdrawal of Vioxx, as well as questions and answers for patients, is available online at <http://www.fda.gov/cder/drug/infopage/vioxx/default.htm>.

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FDA Public Health Advisory: Safety of Vioxx

Merck & Co., Inc. today announced a voluntary withdrawal of Vioxx from the U.S. market due to safety concerns. Vioxx is a prescription COX-2 selective, non-steroidal anti-inflammatory drug (NSAID) that was approved by FDA in May 1999 for the relief of the signs and symptoms of osteoarthritis, for the management of acute pain in adults, and for the treatment of menstrual symptoms. It is also approved for the relief of the signs and symptoms of rheumatoid arthritis in adults and children.

The Agency was informed by Merck & Co., Inc. on September 27, 2004, that the Data Safety Monitoring Board for an ongoing long-term study of Vioxx (APPROVE) had recommended that the study be stopped early for safety reasons. The study was being conducted in patients at risk for developing recurrent colon polyps. The study showed an increased risk of cardiovascular events (including heart attack and stroke) in patients on Vioxx compared to placebo, particularly those who had been taking the drug for longer than 18 months. Based on this new safety information, Merck and FDA officials met the next day, September 28, 2004, and during that meeting FDA was informed that Merck was voluntarily withdrawing Vioxx from the market place.

The risk that an individual patient taking Vioxx will suffer a heart attack or stroke related to the drug is very small. Patients who are currently taking Vioxx should contact their physician for guidance regarding discontinuation and alternative therapies.

FDA is working closely with Merck to coordinate the withdrawal of this product from the U.S. market place. Healthcare professionals are advised to contact Merck at 1-888-368-4699 or at www.merck.com or at the FDA's Drug Information Office at 301-827-4573 or 1-888-463-6332 or go to Vioxx Information on FDA's website at: www.fda.gov/cder/drug/infopage/vioxx/default.com for questions about this product.

Vioxx (rofecoxib) Questions and Answers

1. What action did Merck take today?

Merck announced a voluntary worldwide withdrawal of Vioxx (rofecoxib).

2. What is Vioxx?

Vioxx is a COX-2 selective nonsteroidal anti-inflammatory drug (NSAID). Vioxx is also related to the nonselective NSAIDs, such as ibuprofen and naproxen. Vioxx is a prescription medicine used to relieve signs and symptoms of arthritis, acute pain in adults, and painful menstrual cycles.

3. Did FDA require this action?

No, Merck made this decision independent of input from FDA. The Agency has not had an opportunity to review the data from the study that was stopped in the depth that Merck has, but agrees with the company that there appear to be significant safety concerns for patients, particularly those taking the drug chronically.

FDA plans to work closely with Merck to coordinate the withdrawal of this product from the US market.

4. What action did FDA take today?

FDA issued a public health advisory concerning the use of Vioxx. This advisory is based on Merck & Co., Inc. voluntarily withdrawing Vioxx from the market due to safety concerns.

5. What should I do if I am currently taking Vioxx?

The risk that an individual patient will suffer a heart attack or stroke related to Vioxx is very small. We encourage people taking Vioxx to contact their physician to discuss discontinuing use of Vioxx and alternative treatments. Any decision about which drug product to take to treat your symptoms should be made in consultation with your physician based on an assessment of your specific treatment needs.

6. What are the likely long-term health effects, if any, of taking this product?

The new study shows that Vioxx may cause an increased risk in cardiovascular events such as heart attack and strokes during chronic use.

7. What evidence supports the Public Health Advisory?

Merck's decision to withdraw Vioxx from the market is based on new data from a trial called the APPROVe [Adenomatous Polyp Prevention on VIOXX] trial. In the APPROVe trial, Vioxx was compared to placebo (sugar-pill). The purpose of the trial was to see if Vioxx 25 mg was effective in preventing the recurrence of colon polyps. This trial was stopped early because there was an increased risk for serious cardiovascular events, such as heart attacks and strokes, first observed after 18 months of continuous treatment with Vioxx compared with placebo.

8. Why wasn't the APPROVe trial stopped earlier?

The APPROVe trial began enrollment in 2000. The trial was being monitored by an independent data safety monitoring board (DSMB). It was not stopped earlier because the results for the first 18 months of the trial did not show any increased risk of confirmed cardiovascular events on Vioxx.

9. What did FDA know about the risk of heart attack and stroke when it approved Vioxx?

FDA originally approved Vioxx in May 1999. The original safety database included approximately 5000 patients on Vioxx and did not show an increased risk of heart attack or stroke. A later study, VIGOR (VIOXX GI Outcomes Research), was primarily designed to look at the effects of Vioxx on side effects such as stomach ulcers and bleeding and was submitted to the FDA in June 2000. The study showed that patients taking Vioxx had fewer stomach ulcers and bleeding than patients taking naproxen, another NSAID, however, the study also showed a greater number of heart attacks in patients taking Vioxx. The VIGOR study was discussed at a February 2001 Arthritis Advisory Committee and the new safety information from this study was added to the labeling for Vioxx in April 2002. Merck then began to conduct longer-term trials to obtain more data on the risk for heart attack and stroke with chronic use of Vioxx.

10. Is FDA's expedited review process putting riskier drugs on the market?

No. Vioxx received a six-month priority review because the drug potentially provided a significant therapeutic advantage over existing approved drugs due to fewer gastrointestinal side effects, including bleeding. A product undergoing a priority review is held to the same rigorous standards for safety, efficacy, and quality that FDA expects from all drugs submitted for approval.

11. What other drugs are similar to Vioxx?

Vioxx is a COX-2 selective, nonsteroidal anti-inflammatory drug (NSAID). Other

COX-2 selective NSAIDs on the market at this time are Celebrex (celecoxib) and Bextra (valdecoxib). Vioxx is also related to the nonselective NSAIDs, such as ibuprofen and naproxen. You should consult your physician to determine which treatment is right for you.

12. Does today's action suggest that other drugs in the same class are dangerous?

The results of clinical studies with one drug in a given class do not necessarily apply to other drugs in the same class. All of the NSAIDs have risks when taken chronically, especially of gastrointestinal (stomach) bleeding, but also liver and kidney toxicity. Patients using these drugs for a long period of time (longer than two weeks) should be under the care of a physician.

13. Will Vioxx be recalled?

FDA did not request a recall of Vioxx. This product is being voluntarily withdrawn from the market by Merck.

14. Can my pharmacist continue to fill my prescription for Vioxx?

No, Merck is initiating a market withdrawal in the United States to the pharmacy level. This means Vioxx will no longer be available at pharmacies.

15. How can I report a serious side effect with Vioxx to FDA?

FDA encourages anyone aware of a serious adverse reaction to make a MedWatch report. You can report an adverse event in two ways:

- Visit www.fda.gov/medwatch and click on "How to Report"
- Call 1-800-FDA-1088

16. Where can I get more information?

You can obtain more information from Merck at:

- www.merck.com and www.vioxx.com , or
- 1-888-36VIOXX (1-888-368-4699)

To find out more about Vioxx from FDA:

- Visit our Drug Information web page at: www.fda.gov/cder
- Call Drug Information at: 888-INFO-FDA (888-463-6332)