

No. COX 01-007  
Feb 09, 2001

**Bulletin for VIOXX®:  
FDA Arthritis Advisory Committee Meeting for VIOXX®**

**TO:**

All field personnel with responsibility for VIOXX®  
National Account Executives  
and Customer Managers (All Segments)

Action Required  
Background Information

**DO NOT INITIATE DISCUSSIONS ON THE FDA ARTHRITIS ADVISORY COMMITTEE (ADVISORY COMMITTEE) REVIEW OR THE RESULTS OF THE VIOXX® GI OUTCOMES RESEARCH (VIGOR) STUDY. YOU MAY RESPOND TO CUSTOMER INQUIRIES ONLY AS OUTLINED BELOW.**

**Introduction:**

As previously communicated in June 2000, Merck submitted a supplemental NDA for VIOXX based upon the VIOXX GI Outcomes Research study (VIGOR). In this study, VIOXX 50mg daily significantly reduced the risk of serious gastrointestinal side effects by 54% vs. naproxen 1000mg daily. On Thursday, Feb 8, Merck and the FDA reviewed the study with the FDA's Arthritis Advisory Committee.

The purpose of this bulletin is to provide you with important, updated background information based on the results of this meeting and actions required by you.

**Action Required:**

1. Stay focused on the EFFICACY messages for VIOXX
2. Utilize the PIR system to respond to unsolicited physician inquiries
3. Review the updated background Q&A
4. Review the updated obstacles and responses for your physicians
5. Do not initiate discussions or respond to questions, except as outlined below

**Stay Focused on Efficacy**

It is critical that we remain focused on the 1S HI NSAID and HI COXIB messages for VIOXX with our targeted physicians. As discussed at your 1S District Meetings, both the OA efficacy data and the new acute pain narcotic efficacy data for VIOXX will continue to solidify the efficacy perception of VIOXX. Use the new core visual aid for VIOXX and the

OA Efficacy Stock Bottle Challenge program to challenge physicians to gain experience with the 24 hour efficacy of VIOXX.

**Physician Inquiries:**

In response to unsolicited requests for information regarding VIGOR, Medical Services will make a personalized, faxable PIR available for your customers within 24 hours. In addition, for those customers who request additional information, a separate, more comprehensive PIR packet can be Federal Expressed within 2 days.

Medical Services has made arrangements to extend the hours for the PIR hotline. Representatives should submit unsolicited PIR requests by either telephone or fax options from 2/9 through 2/23 by calling the PIR hotline 800MERCK66 (800-637-2566) during extended hours of 8:30 am to 6:30pm ET. During these hours, a staff member will verbally request the following information from you to process the PIR request from the HCP [After this time, the usual method options of INSIGHT, PIR hotline (800MERCK 66 – hours: 8:30 – 4:30pm ET) and fax can be followed].

**Faxable PIR Instructions:**

- Your name, field title and RDT
- The requesting HCP's full name and professional degree
- HCP's full mailing address
- HCP's phone number
- HCP's FAX number
- Provide the question(s) asked by the HCP.

PIR Requests may also be sent to Medical Services from 4:30 pm – 8:30am ET by leaving a voice message at 800MERCK66. The information as listed above should be provided in your voice message to Medical Services staff. Additionally, PIR requests may be submitted to Medical Services in writing by sending a fax to 800MERCK66. The information listed above should be included on your fax to Medical Services.

**In Summary:**

- If requested, a summary of the PIR will be faxed within 24 hours of receiving the request.
- If the physician requests more comprehensive information on the VIGOR study, you may request the comprehensive PIR. This will be sent via Fed EX within 2 days.
- Transition your discussion to the current strategy and messages for VIOXX®.
- Do not proactively discuss the Advisory Committee Meeting or VIGOR. Respond to questions about the study by requesting a PIR and in accordance with the obstacle-handling guide.

**Updated Q&A Guide:**

This is background information only.



"VIGOR QA.doc"

**Updated Obstacle Responses:**



Obstacles.doc

These updated obstacles are provided for your reference and preparation for questions asked by your physicians.

**This information is provided for your background information *only* and is not to be used in discussions with physicians.**

**Background Information:**

Merck issued a press release summarizing the FDA Advisory Committee Meeting held on Feb 8. The press release is attached below for your background information only:

GAITHERSBURG, Md., Feb. 8, 2001 – The Arthritis Advisory Committee of the Food and Drug Administration today reviewed Merck & Co., Inc.'s application for changes to the prescribing information for Vioxx® (rofecoxib), Merck's medicine for osteoarthritis and acute pain, to reflect results from the Vioxx Gastrointestinal Outcomes Research (VIGOR) study.

The Advisory Committee agreed with Merck and the FDA that results from the study should be included in the labeling for Vioxx. The FDA is not obligated to follow the advice of the Advisory Committee, but usually does. The FDA noted that it will consider all available information, including the information reported and advice received at today's Advisory Committee meeting, before any final decisions are made on Merck's application and other issues discussed by the Committee.

"Merck is confident that the data presented today support the excellent safety profile of Vioxx, and we look forward to further discussions with the FDA to complete the review of our application to modify the labeling for Vioxx," said Eve Slater, M.D., senior vice president, Clinical and Regulatory Development, Merck Research Laboratories.

Vioxx was approved by the FDA in May 1999 to treat osteoarthritis and acute pain. The prescribing information for Vioxx currently contains the standard NSAID Warning about GI side effects. Merck's application to the FDA was based on the 8,000-patient VIGOR

study, which evaluated the GI profile of Vioxx 50 mg compared to the non-selective NSAID naproxen, and on other studies with Vioxx.

In VIGOR, Vioxx 50 mg, a dose two-times the highest chronic dose approved for osteoarthritis, significantly reduced serious GI side effects by half compared to a commonly used dose of naproxen (1,000 mg) in rheumatoid arthritis patients. The Committee recommended that these results be included in the labeling. Vioxx is not indicated for rheumatoid arthritis.

Although the VIGOR study was a GI outcomes study and was not designed to show differences in cardiovascular effects, significantly fewer heart attacks were observed in patients taking naproxen (0.1 percent) compared to the group taking Vioxx 50 mg (0.5 percent) in this study. There was no difference in cardiovascular mortality between the groups treated with Vioxx or naproxen. Patients taking aspirin did not participate in VIGOR.

In extensive discussions, the Advisory Committee explored this finding, other studies of Vioxx and possible explanations for this result in VIGOR. In the completed osteoarthritis trials and on-going clinical trials with Vioxx 12.5 mg, 25 mg and 50 mg in 30,000 patients, there was no difference in the incidence of cardiovascular events, such as heart attacks, among patients taking Vioxx, other NSAIDs and placebo.

Merck scientists said the VIGOR finding is consistent with naproxen's ability to block platelet aggregation by inhibiting COX-1 like aspirin, which is used to prevent second cardiac events in patients with a history of heart attack, stroke or other cardiac events. This is the first time this effect of naproxen on cardiovascular events has been observed in a clinical study. Other explanations were advanced by the FDA reviewer and were discussed with the Advisory Committee. The Committee recommended that the data on cardiovascular events in VIGOR be included in the labeling for Vioxx.

In addition, the Committee agreed that the prescribing information for both Vioxx and Celebrex® (celecoxib) should reflect the fact that neither of these selective NSAIDs confer cardioprotective benefits and are not a substitute for low-dose aspirin. The Committee also recommended that other studies be conducted to further explore the safety of concomitant use of selective NSAIDs and low-dose aspirin.

**Focus:**

**Remain focused on your efficacy messages for VIOXX. Remember that the primary attribute that physicians and patients are seeking is pain relief.**

**For questions regarding this bulletin please contact your Business Manager. For product and service information, call the Merck National Service Center at 1-800-NSC MERCK (1-800-672-6372).**