

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

21-042 / S-002

Trade Name: Vioxx

Generic Name: Rofecoxib

Sponsor: Merck & Co

Approval Date: October 28, 1999

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APPLICATION NUMBER:

21-042 / S-002

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APPROVAL LETTER

HFD 95
(IMAGING)

OCT 28 1999

NDA 21-042/S-002

Merck Research Laboratories
Attention: Eric A. Floyd, Ph.D.
Associate Director, Regulatory Affairs
Sumneytown Pike
P.O. Box 4, BLA-20
West Point, Pennsylvania 19486

Dear Dr. Floyd:

Please refer to your supplemental new drug application dated May 26, 1999, received May 27, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vioxx (rofecoxib tablets) Tablets, 12.5 mg and 25 mg.

We acknowledge receipt of your submissions dated September 22; and October 19, 27, and 28, 1999.

This supplemental new drug application provides for a patient package insert.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text. Accordingly, the supplemental application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling text for the patient package insert.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 21-042/S-002." Approval of this submission by FDA is not required before the labeling is used.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-40
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact Sandra N. Cook, Project Manager, at (301) 827-2090.

Sincerely,

Karen Midthun 10/28/99

Karen Midthun, M.D.
Acting Director
Division of Anti-Inflammatory, Analgesic and
Ophthalmic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Enclosure

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cc:

Archival NDA 21-042

HFD-550/Div. Files

HFD-550/S.Cook

HFD-550/Villalba MW

HFD-550/Midthun/Hyde

HF-2/MedWatch (with labeling)

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HFD-613/OGD (with labeling)

HFD-21/ACS (with labeling)

HFD-095/DDMS-IMT (with labeling)

HFD-830/DNDC Division Director

DISTRICT OFFICE

Drafted by: SNC/October 28, 1999

APPROVAL (AP)

**CENTER FOR DRUG EVALUATION AND
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LABELING

APPROVED

OCT 28 1999

Final Version

**Patient Information about
VIOXX™ (rofecoxib tablets and oral suspension)
VIOXX™ (pronounced "VI-ox")
for Osteoarthritis and Pain
Generic name: rofecoxib ("ro-fa-COX-ib")**

You should read this information before you start taking VIOXX*. Also, read the leaflet each time you refill your prescription, in case any information has changed. This leaflet provides only a summary of certain information about VIOXX. Your doctor or pharmacist can give you an additional leaflet that is written for health professionals that contains more complete information. This leaflet does not take the place of careful discussions with your doctor. You and your doctor should discuss VIOXX when you start taking your medicine and at regular checkups.

What is VIOXX*?

VIOXX is a nonsteroidal anti-inflammatory drug (NSAID) that is used to reduce pain and inflammation (swelling and soreness). VIOXX is available as a tablet or a liquid that you take by mouth.

VIOXX is a medicine for:

- relief of osteoarthritis (the arthritis caused by age-related "wear and tear" on bones and joints)
- management of acute pain in adults (like the short-term pain you can get after a dental or surgical operation)
- treatment of menstrual pain (pain during women's monthly periods)

Who should not take VIOXX?

Do not take VIOXX if you:

- have had an allergic reaction such as asthma attacks, hives, or swelling of the throat and face to aspirin or other NSAIDs (for example, ibuprofen, and naproxen).
- have had an allergic reaction to rofecoxib, which is the active ingredient of VIOXX, or to any of its inactive ingredients. (See Inactive Ingredients at the end of this leaflet.)

What should I tell my doctor before and during treatment with VIOXX?

Tell your doctor if you are:

- pregnant or plan to become pregnant. VIOXX should not be used in late pregnancy because it may harm the fetus.
- breast-feeding or plan to breast-feed. It is not known whether VIOXX is passed through to human breast milk and what its effects could be on a nursing child.

Tell your doctor if you have:

- kidney disease
- liver disease
- heart failure
- high blood pressure
- had an allergic reaction to aspirin or other NSAIDs
- had a serious stomach problem in the past

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Tell your doctor about:

- any other medical problems or allergies you have now or have had.
- all medicines that you are taking or plan to take, even those you can get without a prescription.

Tell your doctor if you develop:

- ulcer or bleeding symptoms (for instance, stomach burning or black stools, which are signs of possible stomach bleeding).
- unexplained weight gain or swelling of the feet and/or legs.
- skin rash or allergic reactions. If you have a severe allergic reaction, get medical help right away.

How should I take VIOXX?

VIOXX should be taken once a day. Your doctor will decide what dose of VIOXX you should take and how long you should take it. You may take VIOXX with or without food.

Can I take VIOXX with other medicines?

Tell your doctor about all of the other medicines you are taking or plan to take while you are on VIOXX, even other medicines that you can get without a prescription. Your doctor may want to check that your medicines are working properly together if you are taking other medicines such as:

- methotrexate (a medicine used to suppress the immune system)
- warfarin (a blood thinner)
- rifampin (an antibiotic)
- ACE inhibitors (medicines used for high blood pressure and heart failure)

What are the possible side effects of VIOXX?

Serious but rare side effects that have been reported in patients taking VIOXX and/or related medicines have included:

- Serious stomach problems, such as stomach and intestinal bleeding, can occur with or without warning symptoms. These problems, if severe, could lead to hospitalization or death. Although this happens rarely, you should watch for signs that you may have this serious side effect and tell your doctor right away.
- Serious kidney problems occur rarely in patients taking NSAIDs.
- Severe liver problems occur rarely in patients taking NSAIDs. Tell your doctor if you develop symptoms of liver problems. These include nausea, tiredness, itching, tenderness in the right upper abdomen, and flu-like symptoms.

More common, but less serious side effects reported with VIOXX have included the following:

Upper and or lower respiratory infection and/or inflammation

Headache

Dizziness

Diarrhea

Nausea and/or vomiting

Heartburn, stomach pain and upset

Swelling of the legs and/or feet

High blood pressure
Back pain
Tiredness
Urinary tract infection

These side effects were reported in at least 2% of osteoarthritis patients receiving daily doses of VIOXX 12.5 mg to 25 mg in clinical studies.

The side effects described above do not include all of the side effects reported with VIOXX. Do not rely on this leaflet alone for information about side effects. Your doctor or pharmacist can discuss with you a more complete list of side effects. Any time you have a medical problem you think may be related to VIOXX, talk to your doctor.

What else can I do to help manage my osteoarthritis pain?

Talk to your doctor about:

- Exercise
- Controlling your weight
- Hot and cold treatments
- Using support devices.

What else should I know about VIOXX?

This leaflet provides a summary of certain information about VIOXX. If you have any questions or concerns about VIOXX, osteoarthritis or pain, talk to your health professional. Your pharmacist can give you an additional leaflet that is written for health professionals.

Do not share VIOXX with anyone else; it was prescribed only for you. It should be taken only for the condition for which it was prescribed.

Keep VIOXX and all medicines out of the reach of children.

Inactive Ingredients:

Oral suspension: citric acid (monohydrate), sodium citrate (dihydrate), sorbitol solution, strawberry flavor, xanthan gum, sodium methylparaben, sodium propylparaben.

Tablets: croscarmellose sodium, hydroxypropyl cellulose, lactose, magnesium stearate, microcrystalline cellulose, and yellow ferric oxide.

Issued XXXX, 1999

MERCK & CO., INC.
West Point, PA 19486, USA

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**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**