CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-647

CHEMISTRY REVIEW(S)

NDA 21-647

Vioxx™ (rofecoxib) Tablets

Merck & Co., Inc.

Martha R. Heimann, Ph.D.
Division of Neuropharmacological Drug Products

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Chemistry Review Data Sheet

1. NDA 21-647

2. REVIEW #: 1

3. REVIEW DATE: February 2, 2004

4. REVIEWER: Martha R. Heimann, Ph.D.

5. PREVIOUS DOCUMENTS: N/A

Previous Documents	Document Date

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original NDA	23-May-2003

7. NAME & ADDRESS OF APPLICANT:

Name:	Merck & Co., Inc.
Address:	Sumneytown Pike, P.O. Box 4, BLA-20 West Point, PA 19486
Representative:	Peter J. Basseches, Ph.D. Director, Regulatory Affairs
Telephone:	(484) 344-7026

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: VIOXX™
b) Non-Proprietary Name (USAN): rofecoxib
c) Code Name/#: MK-0966, L-748731
d) Chem. Type/Submission Priority:
- Chem. Type: 6
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: N/A

10. PHARMACOLOGICAL. CATEGORY: Acute treatment of migraine

11. DOSAGE FORM: Tablets

12. STRENGTH/POTENCY: 12.5 mg, 25 mg and 50 mg tablets

The proposed dosages for treatment of migraine in adults are 25 mg and 50 mg.

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: _X_Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

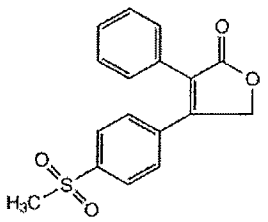
_____SPOTS product – Form Completed

__X__Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical name: 4-[4-(methylsulfonyl)phenyl]-3-phenyl-2-(*5H*)-furanone

Structural formula:



Molecular formula: $C_{17}H_{14}O_4S$

Molecular weight: 314.36

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs: N/A

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
Vioxx Tablets original NDA	NDA 21-042 and supplements	Approval for use in the treatment of osteoarthritis, treatment of rheumatoid arthritis in adults, management of acute pain in adults, and treatment of primary dysmenorrhea.
Vioxx Oral Suspension original NDA	NDA 21-052 and supplements	As for VIOXX Tablets (see above)
VIOXX [redacted] IND	IND 61,419	[redacted]

18. STATUS:

CONSULTS/CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	Not required	---	---
EES	Not required	---	---
Pharm/Tox	Not required	---	---
Biopharmaceutics	Not required	---	---
LNC	Not required	---	---
Methods Validation	Not required	---	---
DMETS	Not applicable. The tradename VIOXX is already in use.	---	---
EA	Claim for categorical exclusion is acceptable	02-FEB-2004	M. Heimann
Microbiology	Not required	---	---

The Chemistry Review for NDA 21-647

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

From the chemistry perspective, approval of this application is recommended.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

No post-approval commitments are required.

II. Summary of Chemistry Assessments

Reviewer Note: This NDA cross-references all CMC information to the approved applications for VIOXX™ Tablets (NDA 21-042) and VIOXX™ Oral Suspension (NDA 21-052). No CMC related changes to the approved products are proposed in this application.

A. Description of the Drug Products and Drug Substance

VIOXX (rofecoxib), which is available as tablets or an oral suspension, is, currently approved for use in the treatment of osteoarthritis, treatment of rheumatoid arthritis in adults, management of acute pain in adults, and treatment of primary dysmenorrhea. In addition to the active ingredient, rofecoxib, VIOXX Tablets, contain the following inactive ingredients: croscarmellose sodium, hydroxypropyl cellulose, lactose, magnesium stearate, microcrystalline cellulose, and yellow ferric oxide. VIOXX Oral Suspension contains the following inactive ingredients: citric acid monohydrate, sodium citrate dihydrate, sorbitol solution, strawberry flavor, xanthan gum, sodium methylparaben (0.13%, preservative), sodium propylparaben (0.02%, preservative).

B. Description of How the Drug Product is Intended to be Used

Vioxx is intended for acute treatment of migraine, with or without aura, in adults. The recommended starting dose is 25 mg; however, some patients may receive additional benefit with a 50 mg dose in comparison to 25 mg. The maximum recommended daily dose is 50 mg. Chronic use of the 50 mg daily dose is not recommended.

12.5 mg and 25 mg VIOXX Tablets. The ——— tablets may, therefore, be used interchangeably.

C. Basis for Approvability or Not-Approval Recommendation

These drug products are currently approved under NDA 21-042 and NDA 21-052. The current application proposes use of the same products for a new indication. No CMC changes have been made to the approved drug substance or drug products. This application does not increase the maximum allowed daily intake of the active moiety.

The applicant claims categorical exclusion on the basis that the concentration of the active moiety will not exceed 1 ppb at the point of entry into the aquatic environment. The claim for categorical exclusion is appropriate.

In view of the approved status of these products, they should also be approved under the current application.

III. Administrative

A. Reviewer's Signature

See electronic signature in DFS.

B. Endorsement Block

See electronic signatures in DFS.

C. CC Block

See DFS.

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

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2/2/04 03:28:10 PM
CHEMIST

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