

CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

NDA 21-530

Chemistry Review(s)

NDA 21-530

Mobic (meloxicam) Oral Suspension

Boehringer Ingelheim Pharmaceuticals, Inc.

Sue-Ching Lin

Review Chemist

**Division of Anti-Inflammatory, Analgesic, and Ophthalmic
Drugs, HFD-550**



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CHEMISTRY REVIEW



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Chemistry Review Data Sheet

1. NDA 21-530
2. REVIEW #: 1
3. REVIEW DATE: 03-May-2004
4. REVIEWER: Sue-Ching Lin
5. PREVIOUS DOCUMENTS: N/A
6. SUBMISSION(S) BEING REVIEWED:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
Original Submission	18-Aug-2003
Correspondence (C)	10-Oct-2003
Amendment (BC)	29-Oct-2003
Amendment (BC)	26-Apr-2004

7. NAME & ADDRESS OF APPLICANT:

Name: Boehringer Ingelheim Pharmaceuticals, Inc.
Address: 900 Ridgebury Road
P.O. Box 368
Ridgefield, CT 06877-0368
Representative: Charles Mazzarella, Manager, Regulatory Affairs
Telephone: (203) 798-5462

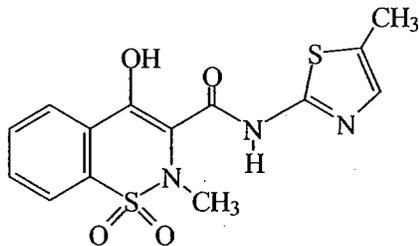
8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: Mobic Oral Suspension
- b) Non-Proprietary Name: meloxicam oral suspension
- c) Code Name/# (ONDC only): UH-AC 62 XX
- d) Chem. Type/Submission Priority (ONDC only):
 - Chem. Type: 3
 - Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505(b)(1)
10. PHARMACOL. CATEGORY: NSAID
11. DOSAGE FORM: suspension
12. STRENGTH/POTENCY: 7.5 mg/5 mL
13. ROUTE OF ADMINISTRATION: oral
14. Rx/OTC DISPENSED: Rx OTC
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
 SPOTS product – Form Completed
 Not a SPOTS product

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

4-Hydroxy-2-methyl-N-(5-methyl-2-thiazolyl)-2H-1,2-benzothiazine-3-carboxamide-1,1-dioxide



CAS 71125-38-7

$C_{14}H_{13}N_3O_4S_2$

M.W. 351.4

Chemistry Review Data Sheet

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
	II	Boehringer Ingelheim	Meloxicam drug substance	1	Adequate	3/2/04	Review #3
	III			4	N/A		See page 44 for details
	III			4	N/A		See page 44 for details
	III			1	Adequate	3/4/04	
	III			3	Adequate	1/7/04	
	III			4	N/A		See page 44 for details
	III			3	Adequate	10/30/00	
	IV			6	N/A		See page 19 for details

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

² Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
IND	51,268	meloxicam
NDA	20-938	Mobic Tablets



CHEMISTRY REVIEW



Chemistry Review Data Sheet

18. STATUS:

ONDC:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	N/A		
EES	Acceptable	10/20/2003	J.D. Ambrogio
Pharm/Tox	N/A		
Biopharm	N/A		
LNC	N/A		
Methods Validation	*		
OPDRA	N/A		
EA	Categorical exclusion (see review)		
Microbiology	N/A		

* The Office of New Drug Chemistry (ONDC) is in the process of revising the method validation process. All review chemists are instructed by ONDC to hold method validation packages and not send to the FDA laboratories until further notice.

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The Chemistry Review for NDA 21-530

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

From a chemistry review perspective, this NDA is recommended for approval.

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

None

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

(1) Drug Substance

The drug substance is meloxicam. Detailed information on the drug substance is referenced to DMF which was recently reviewed by this reviewer on 3/2/04 and found to be adequate to support this NDA. The drug substance was selected to be used in the oral suspension due to its particle size. The meloxicam, which has particle size, was approved for use as the active ingredient of Mobic Tablets (NDA 20-938) on 4/13/2000. The applicant stated that a particle size prevents a rapid sedimentation and therefore provides a suitable period of time for administration of uniform doses.

(2) Drug Product

The drug product is an oral suspension containing 7.5 mg of meloxicam per 5 mL. The meloxicam colloidal silicon dioxide and hydroxyethyl cellulose. The suspending liquid also contains a mixture of purified water, sorbitol, xylitol, glycerol, the sweetener saccharin sodium, and the raspberry flavor, to provide a pleasant taste, particularly for children. The pH of the suspending liquid is at which meloxicam is nearly insoluble and stable.



Executive Summary Section

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

Mobic Oral Suspension will be dispensed by prescription only. It is packaged in a 100-mL amber glass bottle with a child resistant cap. A pour spout intended to prevent inadvertent spillage during dispensing of the suspension is also provided. A clear plastic spoon is provided in the marketed package as a dispensing aid. Mobic Oral Suspension 7.5 mg/5 mL or 15 mg/10 mL may be substituted for Mobic Tablets 7.5 mg or 15 mg respectively, for relief of the signs and symptoms of osteoarthritis.

The submitted stability data include 24-month data for long-term storage conditions and 6-month data for accelerated storage conditions. The stability results support the proposed 24-month expiration period for the drug product stored at controlled room temperature.

C. Basis for Approvability or Not-Approval Recommendation

The CMC information of the drug substance was referenced to DMF [redacted] which was recently reviewed by this reviewer on 3/2/04 and found to be adequate to support this NDA.

The manufacture process, the control of excipients, and the specification are adequate to ensure consistency in the quality of the drug product. The packaging materials were found to be adequate.

The Office of Compliance has issued "acceptable" recommendation for each facility used for manufacturing and control of the drug substance and drug product.

The analytical procedures and the validation of the methods were reviewed and found to be acceptable. Methods validation packages have not been sent to the FDA laboratories because the Office of New Drug Chemistry (ONDC) is in the process of revising the method validation process. According to current CDER policy, the completion of methods validation by the FDA laboratories is not required for determining the approvability of the CMC section.

III. Administrative

- A. Reviewer's Signature: electronically signed in DFS
- B. Endorsement Block: electronically signed in DFS
- C. CC Block: entered electronically in DFS

42 Page(s) Withheld



_____ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

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/s/

Sue Ching Lin
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John Smith
5/7/04 10:22:47 AM
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