CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

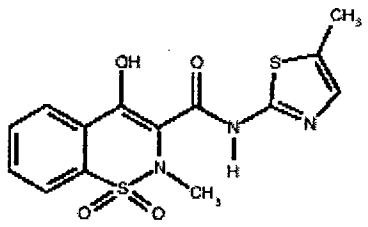
NDA 21-530

Pharmacology Review(s)

Pharmacology /Toxicology Review

NDA 21530
Review number: No. 1
Sequence number/date/type of submission: 0000/August 19, 2003
Information to sponsor: Yes () No (x)
Sponsor and/or agent: Boehringer Ingelheim Pharmaceuticals Inc.
Manufacturer of drug substance:
Reviewer name: Conrad H. Chen, Ph.D.
Division name: Anti-inflammatory, analgesic, and ophthalmic Drug products
HFD#: 550
Review completion date: January 16, 2004
Drug:

Trade name: Mobic, 7.5 mg/5 ml Oral Suspension
Generic name: Meloxicam
Code name: UH AC 62 XX
Chemical name: 4-hydroxy-2-methyl-N-(5-methyl-2-thiazoyl)-2H-1,2-benzothiazine-3-carboxamide-1,1-dioxide
CAS registry number: 71125-38-7
Mole file number:
Molecular formula/molecular weight: $C_{14}H_{13}N_3O_4S_2$/ 351.4
Structure:



Relevant INDs/NDAs/DMFs: NDA 20938 (Mobic 7.5 and 15 mg tablets), approved on April 13, 2000.
Drug class: NSAID
Indication: Relief of the signs and symptoms of osteoarthritis.

Clinical formulation:

Ingredient	Concentration (mg/5 ml)	Concentration (mg/100 ml)	Function	Ref. To Std.
Meloxicam	7.50	150.0	Active drug substance	Company standard
Colloidal Silicon Dioxide				NF
Hydroxyethylcellulose				NF
Noncrystalizing Sorbitol solution				NF
Glycerol				EP
Xylitol				NF
Monobasic sodium phosphate dihydrate				NF
Saccharin sodium				USP
Sodium benzoate				NF
Citric acid monohydrate				USP
Raspberry flavor			Flavoring agent	Company standard
Water purified			Solvent	USP
Total wt. (mg)	5900.00	118,000.0		

Non-clinical study:

The sponsor referred to NDA 20938, Mobic (meloxicam) 7.5 and 15 mg tablets, for the non-clinical information for meloxicam. NDA 20938 was submitted on December 15, 1998 and approved for marketing on April 13, 2000. According to the meeting minutes for pre-NDA 21530 meeting on July 19, 2001, it was decided that no additional non-clinical pharmacology or toxicology studies will be required.

In this submission, the sponsor also submitted the report for a 26-week oral toxicity study in dogs for Metacam (meloxicam) Oral Suspension. The formulation of Metacam Oral Suspension is similar to that of Mobic Oral Suspension. This study was conducted as a requirement of the Center for Veterinary Medicine for a NADA.

The doses used in the 26-week dog study were 0, 0.2, 0.6, and 1.0 mg/kg/day during the first day but reduced to 0, 0.1, 0.3, and 0.5 mg/kg/day for the remaining of the study. The results showed that there were no drug-related changes in ante-mortem, macroscopic, and microscopic examinations.

The proposed human clinical dose of meloxicam is 7.5 to 15 mg a day, which is equal to 0.125 to 0.25 mg/kg/day in a 60 kg body weight person. The human equivalent dose of 0.5 mg/kg/day (the high dose) in dog is 0.5/2 = 0.25 mg/kg/day (based on the inter-species body surface convention). Since the high dose in the 26-week dog study was not more than the maximum human dose, the 'negative' findings of this study would not add additional safety information to meloxicam.

Evaluation and Comment:

Mobic (meloxicam) tablets 7.5 and 15 mg were approved in the United States on April 13, 2000. The sponsor states that meloxicam is currently marketed in over 100 countries. It is marketed outside the United States in tablet, capsule, ampule (for injection), suppository, and oral suspension formulations. In this NDA, the sponsor is applying for the approval of Mobic (meloxicam) Oral Suspension 7.5 mg/5 ml by establishing the bioequivalence between the tablet and the suspension.

No new non-clinical study was submitted. The proposed labeling for Mobic Oral Suspension is similar to that for marketed Mobic Tablet. There is no further non-clinical issue to be addressed. The approval of this NDA is recommended.

Conrad H. Chen, Ph.D.
Reviewing Pharmacologist

Concurrence by: Josie Yang, Ph.D.
Pharmacology Team Leader

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

/s/

Conrad Chen
1/16/04 06:04:32 PM
PHARMACOLOGIST
The approval of this NDA is recommended.
You have seen the hard copy of this review.

Josie Yang
1/20/04 10:57:41 AM
PHARMACOLOGIST