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APPLICATION NUMBER:
22511Orig1s000

CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW(S)

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Office of New Drugs Quality Assessment
BIOPHARMACEUTICS REVIEW - ADDENDUM

NDA#:	22-511/N-000
Submission Date:	03/04/10 (Amendment 0009) and 04/23/10 (Amendment 0014)
Brand Name:	Vimovo
Generic Name:	Naproxen/Esomeprazole
Formulation:	Naproxen Delayed release (DR)/Esomeprazole (Eso) magnesium immediate release (IR) fixed dose combination (FDC) tablets
Strength:	500/20 mg and 375/20 mg
Sponsor:	Pozen
Type of submission:	Amendment to NDA
Reviewer:	Tien-Mien Chen, Ph.D.

SUBMISSION

Reference is made to NDA 22-511 for VIMOVO (naproxen/esomeprazole) 375 mg/20 mg and 500 mg/20 mg Tablets submitted on June 30, 2009, and to the Biopharmaceutics review comments sent to the applicant on April 19, 2010. Reference is also made to the teleconferences held between the applicant and FDA on

1). Feb. 24, 2010, in which the phase 4 commitment on dissolution methodology for VIMOVO Tablets was discussed, and

2). April 21, 2010, in which the dissolution specifications for VIMOVO Tablets on an interim basis (within one year post approval) were discussed.

ADDENDUM

The main objective of this Addendum to the previous Biopharmaceutics Review (in DARRTS dated March 8, 2010) for NDA 22-511 is to document the dissolution specifications that were agreed on with the applicant in the teleconference held on April 21, 2010. Based on this agreement the following dissolution method and specifications will be used on an interim basis for one year for VIMOVO Tablets, 375 mg/20 mg and 500 mg/20 mg.

Acid Stage:

Naproxen only

Acid stage testing determines the acid resistance of the enteric-coated naproxen core tablet.

Dissolution Method

USP Apparatus 2 (with sinkers) at 75 rpm

Medium: 475 mL of 0.1 M HCl at 37°C

Dissolution Specification:

NMT (b) (4) at 2 hours (Meets USP Requirements)

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Buffer Stage:
Esomeprazole and Naproxen
(*Using a second set of tablets***)**

Dissolution Method
USP Apparatus 2 (with sinkers) at 75 rpm
Medium: 900 mL of 0.05 M phosphate buffer pH 7.4 at 37°C

Dissolution Specifications:
Q= (b) (4) at 60 minutes for Naproxen
Q= (b) (4) at 60 minutes for Esomeprazole

Regarding the final dissolution methodology for VIMOVO Tablets, the applicant previous Phase 4 commitment (submitted on March 4, 2010, Sequence #0009) to develop a method to test the naproxen component continuously (i.e. acid then buffer testing on the same set of tablets), remains unaffected. Additionally, the applicant agreed to generate dissolution profile data on multiple batches for both components and submit after one year a proposal for the final dissolution specifications based on the generated data.

_____ 04/24/10, 04/26/10
Tien-Mien Chen, Ph.D. Date
Reviewer
ONDQA Biopharmaceutics

_____ 04/24/10, 04/26/10
Patrick Marroum, Ph.D. Date
ONDQA Biopharmaceutics

CC: NDA
Patrick Marroum, Angelica Dorantes, Tien-Mien Chen

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Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22511	ORIG-1	POZEN INC	PN 400 NAPROXEN/ESOMEPRAZOLE MAGNESIUM

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

/s/

TIEN MIEN CHEN
04/28/2010

PATRICK J MARROUM
04/28/2010

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OFFICE OF CLINICAL PHARMACOLOGY REVIEW

NDA: 22511	Submission Date(s): 06/30/2009
Brand Name	Vimovo®
Generic Name	Naproxen / Esomeprazole Magnesium
Reviewers	PeiFan Bai, Ph.D., Dilara Jappar, Ph.D.
Team Leader	Sue-Chih Lee, Ph.D.
OCP Division	Division of Clinical Pharmacology 3
OND Division	Division of Gastroenterology Products
Sponsor	POZEN Inc
Submission Type; Code	NDA 505 (b) (2), Original
Formulation; Strength(s)	Tablets; EC naproxen 375 mg/IR esomeprazole 20mg; EC naproxen 500 mg/IR esomeprazole 20 mg
Indication	For the treatment of the signs and symptoms of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis in patients at risk for developing NSAID-associated gastric ulcers.
Dosing Regiment	One tablet, twice daily

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