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APPLICATION NUMBER:
22511Orig1s000

PHARMACOLOGY REVIEW(S)

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

FROM: Sushanta Chakder, Ph.D., Supervisory Pharmacologist

DATE: April 13, 2010

Application number: NDA 22,511

Date of submission: June 30, 2009

Sponsor: POZEN Pharmaceutical Development Co.

Drug Product: VIMOVO (Naproxen/Esomeprazole magnesium)

Indication: Treatment of osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis patients at risk of developing NSAID-associated gastric ulcer

Comments:

Under NDA 22511, the sponsor is seeking approval of a combination of naproxen and esomeprazole magnesium for the treatment of osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis patients at risk of developing NSAID-associated gastric ulcer. The only nonclinical study submitted in this NDA application was a pharmacokinetic study in which the urinary and plasma metabolites of buffered and unbuffered omeprazole were determined in female Sprague Dawley rats following 14 days of oral dosing. The NDA was supported by reference to the Agency's previous findings of safety and publicly available information on the toxicology of naproxen and esomeprazole (including omeprazole) to meet the nonclinical assessment requirements.

The nonclinical safety of esomeprazole and naproxen has been established by the respective innovators. During approval of the espmeprazole (Nexium) application, its nonclinical safety was partially based on studies conducted with omeprazole. Following oral administration of omeprazole buffered and unbuffered formulation to female Sprague Dawley rats, the plasma and urinary metabolite profiles for omeprazole were similar. Thus, following oral administration of uncoated esomeprazole, present in VIMOVO, the patients are not expected to be exposed to any new metabolites. Since the mechanisms of action, and the microsomal enzyme systems involved in the metabolism the two components of VIMOVO are not similar, no significant drug-drug interactions between the two components are expected. The sponsor adopted the labeling of the nonclinical sections from the existing labeling of the individual components which is acceptable.

Recommendations:

1. I concur with Dr. Wu's recommendation that there are no additional nonclinical safety concerns for the proposed combination of naproxen and esomeprazole, other than those expected from the individual components.

2. In the nonclinical sections of the labeling (Sections 8.1 and 13.1), the sponsor used headings for reproductive toxicology and carcinogenicity studies of individual components of VIMOVO. These headings should be removed form the labeling.

3. From a nonclinical standpoint, the NDA application is approvable with the recommended changes in the labeling.

_____ _____

Sushanta Chakder, Ph. D. Date
Supervisory Pharmacologist, HDF-180

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/

SUSHANTA K CHAKDER
04/13/2010

DEPARTMENT OF HEALTH AND HUMAN SERVICES
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PHARMACOLOGY/TOXICOLOGY NDA REVIEW AND EVALUATION

Application number:	22511
Supporting document/s:	1
Applicant's letter date:	June 30, 2009
CDER stamp date:	July 1, 2009
Product:	VIMOVO (naproxen/esomeprazole magnesium)
Indication:	Treatment of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis patients at risk for developing NSAID-associated gastric ulcer
Applicant:	POZEN Pharmaceutical Development Co.
Review Division:	Gastroenterology Products
Reviewer:	Charles G. Wu, Ph.D.
Supervisor/Team Leader:	Sushanta Chakder, Ph.D.
Division Director:	Donna Griebel, M.D.
Project Manager:	Anna Simon, MSN, CPNP

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