DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022511 **NDA APPROVAL**

Pozen
Attention: Paul A. Ossi
Senior Vice President, Regulatory Affairs
1414 Raleigh Road
Suite 400
Chapel Hill, N.C. 27517

Dear Mr. Ossi:

Please refer to your New Drug Application (NDA), received June 30, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vimovo (naproxen/esomeprazole magnesium) Delayed Release Tablets, 375 mg/20 mg and 500 mg/20 mg.

We acknowledge receipt of your submissions dated June 30, 2009; August 6, 2009; October 29, 2009; November 11, 13, 19, and 30, 2009; December 18, 2009; March 4, 9, 24, 25, and 26, 2010 and April 23, 28 and 30, 2010.

This new drug application provides for the use of Vimovo (naproxen/esomeprazole magnesium) Delayed Release Tablets, 375 mg/20 mg and 500 mg/20 mg for relief of signs and symptoms of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis, and to decrease the risk of developing gastric ulcers in patients at risk of developing Non-Steroidal Anti-inflammatory Drug (NSAID) associated gastric ulcers.

In our letter dated October 9, 2009, we notified you that a risk evaluation and mitigation strategy (REMS) was required for Vimovo (naproxen/esomeprazole magnesium) to ensure that the benefits of the drug outweigh the risks of cardiovascular and gastrointestinal adverse events. We indicated that your REMS must include a Medication Guide and a timetable for submission of assessments of the REMS.

After consultations between the Office of New Drugs and the Office of Surveillance and Epidemiology, we have reconsidered the need for a REMS for this product. We believe that a Medication Guide is necessary to inform patients of the serious risks of cardiovascular and gastrointestinal adverse events. However, since other drugs currently approved in the non-steroidal anti-inflammatory drug (NSAID) class have Medication Guides with identical safety information regarding these risks that are not included in a REMS, we will not require a REMS.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indications in pediatric patients unless this requirement is waived, deferred, or inapplicable.

For the indication, relief of signs and symptoms of osteoarthritis (OA) and to decrease the risk of developing gastric ulcers in OA patients at risk of developing NSAID-associated gastric ulcers, we are waiving the pediatric study requirement for ages birth to 16 years, 11 months. OA is one of the "adult-related" conditions that does not occur in pediatrics and qualifies for a waiver because studies would be impossible or highly impractical.

For the indication, relief of signs and symptoms of ankylosing spondylitis (AS) and to decrease the risk of developing gastric ulcers in AS patients at risk of developing NSAID-associated gastric ulcers, we are waiving the pediatric study requirement for ages birth to 16 years, 11 months. Necessary studies are impossible or highly impracticable because there are too few pediatric patients with this disease to study. AS typically presents in young adulthood.

For the indication, relief of signs and symptoms of rheumatoid arthritis (RA) and to decrease the risk of developing gastric ulcers in RA patients at risk of developing NSAID-associated gastric ulcers, we are waiving the pediatric study requirement for ages birth to 1 year, 11 months. Necessary studies for pediatric patients in this age range are impossible or highly impracticable because Juvenile Rheumatoid Arthritis (JRA) does not usually present at birth and fewer than 2% of all pediatric visits to a physician for an NSAID prescription for arthritis and arthropathy occur in this age group.

For the indication, relief of signs and symptoms of rheumatoid arthritis (RA) and to decrease the risk of developing gastric ulcers in RA patients at risk of developing NSAID-associated gastric ulcers, we are deferring submission of your pediatric studies for ages 2 to 16 years, 11 months because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the Federal Food, Drug, and Cosmetic Act. These required studies are listed below.

1634-1 Deferred pediatric study under PREA in children 2 years to 11 years of age with Juvenile Rheumatoid Arthritis (JRA)

A safety and population pharmacokinetic (PK) study in children with JRA who are 2 years to 11 years, 11 months of age and require treatment with NSAIDs will be conducted. This study will be a 6 month, multicenter, open-label study to evaluate the dose, safety and PK of VIMOVO in this age group.

Final Report Submission: November 2014

1634-2 Deferred pediatric study under PREA in children 12 years to 16 years and 11 months of age with Juvenile Rheumatoid Arthritis (JRA)

A safety and population pharmacokinetic (PK) study in adolescents with JRA who are ages 12 years to 16 years and 11 months and require treatment with NSAIDs will be conducted. This study will be a 6 month, multicenter, open-label study to evaluate the safety and PK of VIMOVO in this age group.

Final Report Submission: October 2013

Submit final study reports to this NDA. For administrative purposes, all submissions related to these required pediatric postmarketing studies must be clearly designated "**Required Pediatric Assessments**".

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment in your submission dated March 4, 2010. This commitment is listed below.

1634-3 Within one year post-approval, you will transition from the naproxen dissolution test currently in the NDA to the USP method that tests naproxen continuously, i.e. acid followed by buffer, using the same tablet.

Protocol Submission: July 2010
Final Report Submission: April 2011

Submit study protocols to your IND 076301 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each

commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (text for the package insert, and Medication Guide). Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the carton and immediate container labels submitted on March 25, 2010 as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled "Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005)". Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 022511**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

Please submit one market package of the drug product when it is available.

METHODS VALIDATION

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

LETTERS TO HEALTH CARE PROFESSIONALS

If you issue a letter communicating important safety-related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit an electronic copy of the letter to both this NDA and to the following address:

MedWatch
Food and Drug Administration
Suite 12B-05
5600 Fishers Lane
Rockville, MD 20857

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

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