DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-165 **NDA APPROVAL**

Kowa Pharmaceuticals America, Inc.
Attention: John M. Ostrander, PD, PhD
530 Industrial Park Blvd.
Montgomery, AL 36117

Dear Dr. Ostrander:

Please refer to your new drug application dated and received September 27, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cambia (diclofenac) powder for oral solution.

We acknowledge receipt of your submissions dated December 12, 2008, March 12, 2009 and June 16, 2009.

Your December 12, 2008 submission constituted a complete response to our October 27, 2008 action letter.

This new drug application provides for the use of Cambia (diclofenac) powder for oral solution for the acute treatment of migraine attacks with or without aura in adults.

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 agreed-upon labeling text.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENT

Section 505-1 of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require the submission of a Risk Evaluation and Mitigation Strategy (REMS) if FDA determines that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)).

In accordance with section 505-1 of FDCA, as one element of a REMS, FDA may require the development of a Medication Guide as provided for under 21 CFR Part 208. Pursuant to 21 CFR Part 208, FDA has determined that Cambia (diclofenac) poses a serious and significant public health concern requiring the distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of Cambia (diclofenac). FDA has determined that Cambia (diclofenac) is a product that has serious risks (relative to benefits) of which patients should be made aware because information concerning the risks could affect patients' decisions to use, or continue to use Cambia (diclofenac). Under 21 CFR 208, you are responsible for ensuring that the Medication Guide is available for distribution to patients who are dispensed Cambia (diclofenac).

Your proposed REMS, submitted on December 12, 2008 in an electronic communication, and appended to this letter, is approved. The REMS consists of the Medication Guide included with this letter and the timetable for submission of assessments of the REMS.

Your assessment of the REMS should include an evaluation of:

a. Patients' understanding of the serious risks of Cambia (diclofenac)
b. A report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24
c. A report on failures to adhere to distribution and dispensing requirements, and corrective actions taken to address noncompliance

You should submit the final methodology and content of the patient survey at least 90 days prior to initiating the conduct of the survey.

The requirements for assessments of an approved REMS under section 505-1(g)(3) include, in section 505-1(g)(3)(B) and (C), requirements for information on the status of any postapproval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)(vii) and including any updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in 505-1(g) could result in enforcement action.

We remind you that in addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in Section 505-1(g)(2)(A) of FDCA.

Prominently identify submissions containing REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission:

NDA 22-165 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 22-165
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT FOR (NEW INDICATION FOR USE)
FOR NDA 22-165
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send 5 copies of REMS-related submissions.

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 indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric requirement for ages 0 months to up to 6 years because necessary studies are impossible or highly impracticable in that age group. In addition, we are deferring submission of your pediatric studies for ages 6 years to 17 years because this product is ready for approval for use in adults and the pediatric studies have not been completed.

The findings in adults, and on which the current approval is based, demonstrate sufficient safety to proceed with pediatric studies in children ages 12 years to 17 years. Pediatric studies in children ages 6 years to up to 11 years should be delayed until additional safety and effectiveness data have been collected in older children.

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

1. Deferred safety and pharmacokinetic pediatric study under PREA in pediatric patients with migraine with or without aura ages 12 years to 17 years.

   Final protocol submission: by December 2009
   Clinical Trial Start Date: by May 2010
   Final Report Submission: by June 2013

2. Deferred controlled effectiveness study under PREA for the acute treatment of migraine attacks with or without aura in pediatric patients ages 12 years to 17 years.

   Final protocol submission: by December 2010
   Clinical Trial Start Date: by June 2011
   Final Report Submission: by June 2013

3. Deferred long-term open label safety study in pediatric patients with migraine with or without aura ages 12 years to 17 years.

   Final protocol submission: by December 2010
   Clinical Trial Start Date: by June 2011
   Final Report Submission: by June 2013

4. Deferred safety and pharmacokinetic pediatric study under PREA in pediatric patients with migraine with or without aura ages 6 years to 11 years. Upon review of additional safety and effectiveness data in pediatric patients ages 12 to 17 years, we will make a determination as to whether or not pediatric studies are practicable for this age range.

Final protocol submission: by June 2013
Clinical Trial Start Date: by December 2013
Final Report Submission: by December 2016

5. Deferred controlled effectiveness study under PREA for the acute treatment of migraine with or without aura in pediatric patients ages 6 years to 11 years. Upon review of additional safety and effectiveness data in pediatric patients ages 12 to 17 years, we will make a determination as to whether or not pediatric studies are practicable for this age range.

   Final protocol submission: by June 2014
   Clinical Trial Start Date: by December 2014
   Final Report Submission: by December 2016

6. Deferred long-term open label safety study under PREA in pediatric patients with migraine ages 6 years to 11 years. Upon review of additional safety and effectiveness data in pediatric patients ages 12 to 17 years, we will make a determination as to whether or not pediatric studies are practicable for this age range.

   Final protocol submission: by June 2014
   Clinical Trial Start Date: by December 2014
   Final Report Submission: by December 2016

Submit final reports to this NDA 22-165. For administrative purposes, all submissions related to these required pediatric postmarketing studies must be clearly designated "**Required Pediatric Assessment(s)**".

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to enclosed labeling (text for the package insert, text for the patient package insert, text for the Medication Guide). These revisions are terms of the NDA approval. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission "SPL for approved NDA 22-165." We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the carton and immediate container labels submitted on June 16, 2009, 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 22-165." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product(s) 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(s) 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(s), 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 www.fda.gov/cder/ddmac.

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

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 12B05
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).

If you have any questions, call Lana Chen, Regulatory Project Manager, at (301) 796-1056.

Sincerely,

{See appended electronic signature page}

Russell Katz, M.D.
Director
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure

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

/s/

Russell Katz

6/17/2009 03:35:26 PM