CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-165

SUMMARY REVIEW

MEMORANDUM

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Food and Drug Administration

Date:	June 16, 2009
From:	Eric Bastings, MD.
To:	NDA 22-165 file
Subject:	Second cycle CDTL memorandum

NDA 22-165 was issued a complete response (CR) letter on 10/27/2008, for the following reasons (please refer to my first cycle CDTL memorandum for description of the issues in greater detail):

1. Insufficient information to allow adequate product labeling. The division acknowledged that the sponsor had conducted a search of the published literature, but noted that the sponsor had limited the search to the years 2004-2007. At the same time, the division was aware of additional published studies that provided information on the potential for diclofenac to induce developmental toxicity, some or all of them not presented in the sponsor's search.

2. A Medication Guide was requested as part of a Risk Evaluation and Mitigation Strategy (REMS). The division noted that the sponsor had submitted a Medication Guide on October 6, 2009, and that the review of that Medication Guide was ongoing at the time of action.

In a 12/12/2008 response to our CR letter, the sponsor submitted the requested literature search, and a proposed REMS including a Medication Guide.

Non Clinical Review
Dr. Charles Thompson reviewed the non clinical information submitted in this second cycle. Dr. Thompson concluded that none of the published studies warranted description in labeling, and recommended approval. Dr. Lois Freed, supervisory non clinical reviewer, conducted a separate review of the most relevant studies provided by the sponsor, as well as others that she identified in her own literature search, and came to the same conclusions. Dr. Freed provided several labeling recommendations (taking into account recommendations from the Pediatric and Maternal Health Staff), described in her memorandum, and which I concur with.

Risk Evaluation and Mitigation Strategy
Robin Duer, RN, MBA, from the Division of Risk Management (DRISK) reviewed the proposed Risk Evaluation and Mitigation Strategy. DRISK found that the sponsor's proposed REMS for CAMBIA generally meets the statutory requirements outlined in 21 CFR 208 and in accordance with 505-1. DRISK provided several comments and recommendations, including revisions to the proposed REMS, that were transmitted to

the sponsor and agreed upon. In particular, the sponsor was reminded to comply with 21 CFR 208.24, as follows:

- A required statement alerting the dispenser to provide the Medication Guide with the product must be on the carton and container of all strengths and formulations.
- Sufficient numbers of Medication Guides should be provided with the product such that a dispenser can provide one Medication Guide with each new or refilled prescription.
- The sponsor should submit for review a detailed plan to evaluate patients' understanding about the safe use of CAMBIA (diclofenac potassium for oral solution) at least 2 months before they plan to conduct the evaluation.

The sponsor agreed to comply with these requirements.

Medication Guide
Robin Duer (DRISK) and Sharon Watson (DDMAC) reviewed the Medication Guide. I integrated DDMAC comments to the DRISK revised document. The sponsor agreed to the proposed changes.

Tradename
Dr. Laura Pincock from the Division of Medication Error Prevention and Analysis (DMEPA) reviewed the proposed tradename, CAMBIA, and found it acceptable.

Carton and Container
DMEPA also reviewed the Cambia packet labels and carton labeling, and provided several comments, as follows:

- Increase the prominence of the strength and state the strength as "50 mg per packet" on all labels and labeling.
- Relocate the 'Rx Only' statement away from the strength. We suggest relocating to the bottom left corner of the principal display panel of the carton or the packet.
- Rephrase the net quantity statement on the carton to read: "Contains 9 packets". Referring to the packets in term of sets (e.g., three sets of three packets each) can imply that the dose is comprised of more than one packet or a 'set'.
- (b) (4).

(b) (4)

(b) (4)

Recommendation: I recommend approval, as all outstanding issues have been resolved.

Eric P. Bastings, M.D.
Deputy Division Director, Neurology

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/s/

Eric Bastings
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MEDICAL OFFICER