CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-251

PHARMACOLOGY REVIEW(S)

September 12, 2008

Review and Evaluation of Pharmacology and Toxicology
Original NDA Review

NDA: 22-251

Sponsor: GlaxoSmithKline
Research Triangle Park, NC

Rec'd: 11/28/07

Drug: Lamictal (lamotrigine) Orally Disintegrating Tablet (ODT)

Indication: Epilepsy

Related NDA: NDA 20-241 (Lamictal Tablet)

Summary and Evaluation:

No pharmacology or toxicology studies were submitted to this NDA for an ODT form of lamotrigine, which relies on preclinical data previously submitted for the IR tablet (20-241). The basis for approval of Lamictal ODT is bioequivalence with the approved formulation of lamotrigine. There are no unusual excipients or new degradation products in the ODT formulation and no additional safety concerns associated with the dosage form with the exception of polyethylene (PE) which is used to coat the drug particles to mask taste. This was initially thought to pose a problem, since the toxicity data provided by the sponsor to support its safe use was inadequate. However, subsequent information provided in response to chemistry requests proved adequate to support the safety of the levels of PE used in the ODT. Otherwise, the specification limits are very similar and the maximum dose is the same for both formulations. Therefore, the pharmacology/toxicology data submitted by GSK to the previous NDA support approval of the ODT for the same indication. Labeling revisions are included below.

(b) (4)

[redacted]

Non-Teratogenic Effects: As with other AEDs, physiological changes during pregnancy may affect lamotrigine concentrations and/or therapeutic effect. There have been reports of decreased lamotrigine concentrations during pregnancy and restoration of pre-partum concentrations after delivery. Dosage adjustments may be necessary to maintain clinical response.

(b) (4)

[redacted]

NDA (22-251)
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J. E. Fisher, Ph.D.

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/s/

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9/12/2008 02:00:31 PM
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