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APPLICATION NUMBER:

22-267

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-168 / S-015
NDA 22-267

Abbott Laboratories
Attention: Steven F. Hoff, R.Ph., Ph.D.
Associate Director
Global Pharmaceutical Regulatory Affairs
200 Abbott Park Road
PA76, Building AP-30-1E
Abbott Park, Illinois 60064-6157

Dear Dr. Hoff:

Please refer to your supplemental new drug application submitted September 24, 2007, received September 24, 2007 under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Depakote ER (divalproex sodium extended-release tablets) 250 mg and 500 mg. Please also refer to your new drug application submitted September 24, 2007, received September 24, 2007 under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Depakote ER (divalproex sodium extended-release tablets) 250 mg and 500 mg.

Your supplemental NDA [21-168 / S-015] provided a response to the Agency's Pediatric Written Request, dated August 9, 2002, revised May 7, 2004 and December 21, 2005, and reissued January 31, 2006, for Depakote ER in pediatric migraine. Your NDA [22-267] provided a response to the Agency's Pediatric Written Request, dated August 9, 2002, revised May 7, 2004 and December 21, 2005, and reissued January 31, 2006, for Depakote ER in mania associated with bipolar disorder in children and adolescents.

Please also refer to your amendments to both NDA 21-168 / S-015 and NDA 22-267, dated October 31, 2007, November 14, 2007, and December 12, 2007.

We have completed the review of NDA 22-267 as amended, and it is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling, unless we notify you otherwise.

Postmarketing Commitment (PREA) Fulfilled; NDA 21-168 / S-012. The substantive review of NDA 21-168 / S-015 is being addressed by the Division of Neurology Products. However, this supplemental application is cross-referenced to NDA 22-267 with respect to reports on the following postmarketing study commitment, established under the Pediatric Research Equity Act

[PREA], and relevant to approved supplemental application 21-168 / S-012 for Depakote ER in the treatment of bipolar disorder in adults:

> Commitment #1. You are required to assess the safety and effectiveness of Depakote ER in the treatment of bipolar disorder in pediatric patients ages 10 to 17 (children and adolescents).
>
> Final Report Submission: October 7, 2007

Our December 6, 2005 approval letter for NDA 21-168 / S-012 also waived this required study commitment for children aged 0 to 10 years.

We have concluded that the cross-referenced reports under NDA 21-168 / S-015 fulfill the above referenced postmarketing study commitment for NDA 21-168 / S-012.

Pediatric Research Equity Act (PREA) Requirements: Phase 4 Commitments.
All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred.

NDA 22-267 does not provide for any claims that would require further pediatric studies under PREA, nor are any other Phase 4 commitments required for this submission.

Submission of Final Labeling. As noted above, supplemental application S-015 to NDA 21-168, submitted and received September 24, 2007, will be acted upon by the Division of Neurology Products. It is our understanding that this application, when approved, will provide for specific amendments to the labeling for Depakote ER related to pediatric migraine.

Therefore, if NDA 21-168 / S-015 is approved within 30 days of the date of this letter, we request that you submit final printed labeling (FPL), reflecting the combined labeling changes under NDA 21-168 / S-015 and NDA 22-267, to both applications.

Content of Labeling: Structured Product Labeling [SPL]. As soon as possible, but no later than 14 days from the date of this letter [or the date of approval of labeling under NDA 21-168 / S-015, whichever comes later], 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 the enclosed agreed-upon labeling text. 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 labeling under 22-267".

If you issue a letter communicating important information about this product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to NDA 22-267 and to NDA 21-168, with a copy to the following address:

MEDWATCH, HFD-410
Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266

Reporting Requirements. All 15-day alert reports, periodic (including quarterly) adverse drug experience reports, field alerts, annual reports, supplements, and other submissions should be addressed to the original NDA 21-168 for this drug product, not to this NDA. In the future, do not make submissions to this NDA except for the final printed labeling requested above.

If you have any questions, please call Doris J. Bates, Ph.D., Regulatory Project Manager, at 301-796-1040.

Sincerely,

{See appended electronic signature page}

Thomas P. Laughren, M.D.
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure: agreed-upon labeling.

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

/s/

Thomas Laughren
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