CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

21-168

Pharmacology Review(s)

August 1, 2000

Review and Evaluation of Pharmacology and Toxicology
Original NDA Review

NDA: 21-168

Sponsor: Abbott Laboratories
Abbott Park, IL

Rec'd: 10/04/99

Drug: Depakote ER (Divalproex Sodium Extended Release) Tablets

Indication: Migraine

Related NDAs: NDA 18-081 (Depakene [valproic acid] Capsules); NDA 18-723 (Depakote [divalproex sodium] Tablets)

Summary and Evaluation:

No pharmacology or toxicology studies were submitted to this NDA for a new formulation of Depakote, which relies on preclinical data previously submitted for oral dosage forms of valproic acid (VPA) and divalproex sodium. This data was considered adequate to support the initial approval of these agents for the treatment of epilepsy (above referenced NDAs). VPA is associated with a number of serious toxicities, and the risk/benefit assessment would be quite different for the current, less serious indication; but this became a clinical decision, and divalproex sodium was subsequently approved for migraine as well as for mania. (The maximum recommended dose for migraine [1000 mg/day] is below that for epilepsy and mania [60 mg/kg/day].) There are no unusual excipients in the new formulation and no additional safety concerns associated with the extended release profile. Therefore, the pharmacology/toxicology data submitted by Abbott to previous NDAs for oral valproic acid and divalproex sodium support approval of the ER dosage form. Recommended labeling changes are attached.

/S/

E. Fisher, Ph.D.

NDA (21-168)
Div File
HFD-120/GFitzgerald/EFisher/LChen

/S/ 8/3/00

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