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RESEARCH**

APPLICATION NUMBER:

22-267

CHEMISTRY REVIEW(S)

CMC Memo

OND Division: Division of Psychiatry Products
NDA: 22-267
Applicant: Abbott Laboratories
Letter Date: 24-SEP-07
Stamp Date: 24-SEP-07
PDUFA Date: 24-MAR-08
Trademark: Depakote ER
Established Name: divalproex sodium
Dosage Form: Extended Release Tablets (250 & 500 mg)
Route of Administration: Oral
Indication: Pediatric Use in Bipolar Disorder
Assessed by: Thomas F. Oliver, Ph.D.

Depakote ER® (divalproex sodium) is an anticonvulsant approved for the prophylactic treatment of migraine headaches in adults, the treatment of acute manic or mixed episodes associated with bipolar disorder, and for both mono-therapy and adjunctive therapy in complex partial seizures, complex absence seizures and adjunctively for multiple seizure types. Depakote ER® (NDA 21-168) was approved August 4, 2000. Depakote ER® is available as 250 and 500 mg extended release strength tablets.

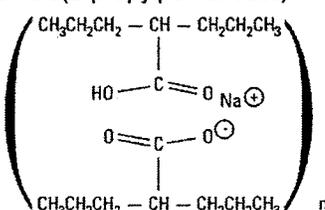
On August 9, 2002, the Agency issued a pediatric Written Request to Abbott Laboratories, requesting the applicant to conduct efficacy and safety pediatric studies of Depakote ER® tablets in patients with bipolar, migraine prophylaxis and epilepsy, and submit information from the pediatric studies. The sponsor has now submitted the requested pediatric epilepsy and migraine trial data in supplemental NDA 21-168 (SE5-015). In addition, the applicant has also submitted data from the completed bipolar studies under NDA 22-267. There was no new CMC information submitted in NDA 22-267, just response to the WR. Please refer to CMC reviews under NDA 21-168.

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/s/

Thomas Oliver
3/6/2008 08:21:36 AM
CHEMIST

Ramesh Sood
3/6/2008 12:11:28 PM
CHEMIST

CHEMIST'S REVIEW #1		1. ORGANIZATION ONDQA/DPE/Branch VII		2. NDA NUMBER 19-680 21-168	
3. NAME AND ADDRESS OF APPLICANT (<i>City and State</i>) Abbott Laboratories/GPRA Dept. RA76/Bldg. AP30-1E 200 Abbott Park Road Abbott Park, IL 60064-6157				4. AF NUMBER	
				5. SUPPLEMENT (S) NUMBER(S) DATES(S)	
6. NAME OF DRUG Depakote Sprinkle Capsules (19-680) Depakote ER (21-168)		7. NONPROPRIETARY NAME Divalproex Sodium		SE5-024 SE5-015	09-24-2007 09-24-2007
8. SUPPLEMENT PROVIDES FOR: the use of Depakote Sprinkle Capsules (19-680) or Depakote ER Tablets (21-168) for the Treatment of Mania Associated with Bipolar Disorder in Children and Adolescents.				9. AMENDMENTS DATES	
10. PHARMACOLOGICAL CATEGORY Anitconvulsant		11. HOW DISPENSED RX <input checked="" type="checkbox"/> OTC		12. RELATED IND/NDA/DMF	
13. DOSAGE FORM(S) Capsules (19-680) Tablets (21-168)		14. POTENCY 125 mg 250 mg, 500 mg			
15. CHEMICAL NAME, STRUCTURE, MOLECULAR FORMULA AND MOLECULAR WEIGHT sodium hydrogen bis(2-propylpentanoate)				16. RECORDS AND REPORTS CURRENT YES__ NO REVIEWED YES__ NO	
					
17. COMMENTS The above two efficacy supplements were submitted in response to a formal written request from the Agency to provide results from studies in pediatric patients. The objective of this study was to compare the safety and efficacy of Depakote Sprinkle Capsules or Depakote ER tablets to placebo in the treatment of bipolar I disorder, manic or mixed episode, in children and adolescents. The results of the studies indicate that neither of the two drug products showed evidence of efficacy when compared to Placebo. No changes are proposed to the description, dosage and administration and how supplied sections of the labeling. The applicant has submitted a claim for categorical exclusion from filing an EA document under 21 CFR 25.31 (b). The applicant's claim is found to be acceptable.					
18. CONCLUSIONS AND RECOMMENDATIONS Provided information is found to be adequate. The above two supplements are recommended for approval from the standpoint of chemistry, manufacturing and controls.					
19. REVIEWER					
NAME Nallaperumal Chidambaram, Ph.D.		SIGNATURE			DATE COMPLETED 03-21-2008
DISTRIBUTION	ORIGINAL NDA	DIVISION FILE	Reviewer: N. Chidambaram Ph.D.	CSO: S. Daugherty HFD-120	Branch Chief: James D. Vidra Ph.D.

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/s/

Nallaperumal Chidambaram
3/21/2008 12:56:42 PM
CHEMIST

Hasmukh Patel
3/21/2008 01:01:31 PM
CHEMIST
Signed off for Dr. James Vidra.