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Prescribing decisions should be made based on the approved package insert in the country of prescription

Sponsor/company:	sanofi-aventis	**ClinialTrials.gov Identifier:**	NA
Generic drug name:	Valproate Acid/Valproate semisodium	**Study Code:**	L_8979
		Date:	31/Aug/2007

Title of the study:	**Randomized, Double-blind, parallel comparison efficacy and safety study of Depakine chrono tablet versus lithium salt in manic phase of bipolar disorder Chinese patients. L_8979**
Investigator(s):	PI: Shu Liang Coordinating investigators: The Sixty hospital of peking university:Prof. zhang Hongyan Beijing Anding hospital: Prof. Ma Xin Beijing huilongguan hospital: Prof. Zhang xinli Guangzhou psychiatry hospital: prof. Guo Yangbo Hunan xiangya hospital: Prof. Zhao Jingping The first hospital of huaxi university: Prof. Sun Xueli Nanjing psychiatry hospital: Prof. Fan Jianxiong Wuhan people hospital: Wang Gaohua The first hospital affiliated Kunming medical college: Prof. Xu Xiufeng The first hospital of Xi'an jiao tong university: Prof. Gao Chenge
Study center(s):	The Sixty hospital of peking university Beijing Anding hospital Beijing huilongguan hospital Guangzhou psychiatry hospital Hunan xiangya hospital The first hospital of huaxi university Nanjing psychiatry hospital Wuhan people hospital The first hospital affiliated Kunming medical college The first hospital of Xi'an jiao tong university

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Study period: Date first **patient/subject** enrolled: 10-02-2004 Date of first signed informed consent Date last **patient/subject** completed: 31-05-2005 Date of last patient last visit	**Phase of development:** Phase II
Objectives:	To assess the efficacy and safety of Depakine Chrono tablet versus Lithium salt in manic phase of bipolar disorder Chinese patients.

Methodology:	This is a randomized, double-blind, active drug parallel comparison and multi-centers clinical study. The patients were divided into the Depakine and the Lithium Carbonate treatment group. The administration dose is 1000-2000mg/d and 1000-2000mg/d respectively in Depakine and Lithium Carbonate group. Patients all accepted 4 weeks treatment period, and the curative effect and safety analysis were performed at the end of the 1st week ,2st week, 3st week and 4st week. The evaluable index of curative effect included the YMRS? BPRS? HAMD GAS and CGI score in the various visit time. The safety analysis was performed in the FAS population, including all AE of various visit time, physical exam, vital sign, clinical lab exam and ECG in baseline and at the end of the trial.		
Number of patients/subjects:	Planned: 240	Randomized: 157	Treated: 156
Evaluated:	Efficacy/Pharmacodynamics: 122	Safety: 156	
Diagnosis and criteria for inclusion:	1. Signed informed consent; 2. Aged 18-65 years old; 3. According with DSM-IV manic phase of bipolar?disorder criteria ; 4. YMRS=20 at screening and baseline time ; 5. The time which psychiatric drug cleaning needed to achieve the re-question ; 6. Subjects considered by the investigator to be likely to comply with the protocol; 7. Menopause female patients; women who are fertile must use a medically acceptable contraceptive and Pregnancy test must be negative; 8. Normal Renal and Liver function; the other test = 1.5 times upper limit of the normal range.		
Investigational product: Dose: Administration:	Depakine Chrono 500mg/ tablet D1: oral 500mg/d, D3: oral 1000mg/d , D7: oral 1500-2000mg/d.		
Duration of treatment: All patients accepted 4 weeks treatment period		**Duration of observation:** 4 weeks	
Reference therapy: Dose: Administration:	Lithium Carbonate tablet 250mg/tablet D1: oral 500mg/d , D3: oral =1000mg/d , D7: oral =2000mg/d.		
Criteria for evaluation:			
Efficacy:	**Primary**: The YMDS score change from the baseline, the efficacy rate (50%), the 30%, 50% and 80% improvement of YMRS score at endpoint was used to be the primary evaluation criterion, **Secondary**: BPRS, HAMD, CGI and GAS were used to be the secondary evaluation criterion.		

Safety:	AE and SAE report in the treatment period.
Statistical methods:	The primary efficacy analysis data was FAS, and also analyzed the PPS population meanwhile. The primary and secondary efficacy data scarcities were deal with by LOCF method. The primary efficacy analysis was the comparison of YMRS score by ANCOVA in considering the centers, groups and their interactions, and performed the No infection test in the primary efficacy points of the two groups. The safety analysis was performed in the FAS population, including all AE, physical exam, vital sign, ECG, clinical lab exam and etc. The lab results adopted by two-side ANOVA test in considering the centers, groups and their interaction to compare the original points in follow-up visits and the variety of pre-treat and post-treat, adopted two-paired t'test to compare the difference of endpoint and baseline in their own group.
Summary:	
Efficacy results:	The clinical results confirmed that Depakine (1000 - 2000 mg/day) of 4 weeks therapy was efficacious in treatment the manic phase of bipolar disorder patients. The primary efficacy analysis-YMRS score reduced to 19.94 and 20.34 respectively in Depakine and Lithium Carbonate group by analysing the FAS, and no significant statistical differences were observed. The 30% decreasing of YMRS score was 81.82% and 78.48% in Depakine and Lithium Carbonate group respectively, no significant difference were shown in the two groups. The secondary efficiency analysis further supported the aforesaid conclusions.
Safety results:	Depakine (1000 - 2000 mg/day) is safe and tolerable well in treatment manic acute episode of bipolar disorder patients.The relative drug AE were 29 times (21.79%) and 23 times (22.78%) respectively in 156 subjects of this study, eight subjects withdraw due to AE (Depakine: 2 times; Lithium Carbonate: 6 times), one SAE happened in Lithium Carbonate treatment group, and no significance difference were observed in the two groups. The more common AEs are gastrointestinal and central nervous system events, most AEs were mild and transient. The common AE was vomiting (6.41%) and nausea (5.13%) in Depakine group.
Date of report:	28-10-2005