April 23, 1967

PHARMACOLOGIST REVIEW OF NDA 16-603

Original Summary

Sponsor: Geigy Chemical Corporation
Ardsley, New York 10502
(AF 25-403)

Related IND: Same sponsor [redacted]

Trade Name: Tegretol

Chemical Name: 5H-dibenz-(b,f)-azepine-5-carboxamide

Trade Name other than Principal Name: Carbamazepine

Dosage Forms: Tablet--200 mg.

Toxicity Studies:

This agent has been the subject of extensive review in the past under its IND ([redacted]). Refer to Dr. J. L. Wilson's reviews of March 26, 1964 and October 10, 1964 and Dr. T. M. Farber's reviews of October 4, 1966, November 2, 1966 and January 25, 1967 for the complete evaluation of the pharmacology and toxicology of this agent.

EVALUATION

As expressed in our previous evaluations in the summaries of October 4, 1966 and November 2, 1966, it is our opinion that the data submitted by the sponsor does not support the safety of Tegretol at the dosage levels recommended in the labeling. Tegretol would appear to be an agent that might possess significant toxicity based on the animal toxicity findings seen to this date. Final action on this application must await the decision of a medical officer who will have to weigh the possible derived benefits against the possible hazards.

In regard to the proposed labeling, we feel that the section on animal toxicity studies does not adequately convey to the physician the fact that Tegretol has little or no margin of safety based on the animal studies performed. There is an overall attempt by the sponsor to reduce the significance of the findings of toxicity in the experimental animals and we feel that a clear statement of this agent's toxic potential is called for. A meeting with the sponsor to clear up the inadequacies in the labeling is indicated.

Theodore M. Farber, Ph.D.
Division of Neuropharmacological Drugs

cc:
Orig NDA
Dup NDA
Trip NDA
CMD
CMD/DND
CSS
DND/TMFarber:jc
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