

Herbert L. Ley, Jr., M.D.
Director, Bureau of Medicine

January 30, 1968

Director, Office of New Drugs

NDA 15-608 -- Tegretol (carbamazepine) Tablets

This product, which is marketed in a number of countries as an anticonvulsant, has been investigated for its effects in the treatment of trigeminal neuralgia. The data submitted have been reviewed by the chemist, medical officer and pharmacologist and discussed with the Division director and with this Office.

The data submitted support the efficacy for the above indication. The toxicity of the drug is fully reflected in the labeling and the Warnings and Precautions are adequate to enable the practitioner to prescribe this drug.

The labels and controls for this application are satisfactory. Approval of this application is recommended.

Robert M. Hodges, M.D.

cc:
NDA 15-608 Orig., Dup., Trip
M-100 CND
M-120 DND)
M-14

RMHodge :pas 1/30/68

*File in
Regulatory*

February 27, 1968

MEDICAL OFFICER REVIEW OF NDA 16-608, Tegretol

I have reviewed the final printed labeling and the changes recommended for the draft labeling have been incorporated into it. (See our approvable letter of February 6, 1968).

The New Drug Application is now ready for final approval and I recommend that the approval letter be sent to Ceigy Pharmaceuticals.

Morris A. Weinberger

Morris A. Weinberger, M.D.

cc:
Dup FDA
Trip NDA
M-100
M-120
M-330
M-125/MAWeinberger/exc
2/27/68

NDA 17-608

Ardsley NY (AF 25-403)

October 9, 1967

MEMORANDUM OF TELEPHONE CONVERSATION

Between: Dr. Edward C. McKeon - Geigy Chemical Corporation

and

Morris A. Weinberger, M.D. - Medical Officer
DND/ONS M-120

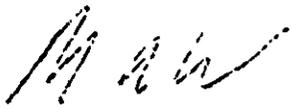
Subject: Eye Studies on Patients treated with Tegretol approximately
Six Months or Longer.

Dr. McKeon called while I was out and I returned his call at 3:50 pm
on October 9, 1967.

He informed me that eye examinations had been completed in 25 patients
who had received Tegretol and in 100 controls. The preliminary results
indicated no abnormalities attributable to treatment with Tegretol.
He informed me that the reports would be hand-carried to FDA, Bureau of
Medicine, by staff members in order to expedite the processing of the
NDA.

He was assured that the reports would be reviewed promptly upon receipt
and, if the eye studies demonstrated no drug effect, then it was stated
that the only further steps necessary for new drug approval would be
checking of the chemical controls and the revised labeling. After the
new data were reviewed, a meeting would be arranged to settle the
previously mentioned items.

This concluded the conversation.


Morris A. Weinberger, M.D.

cc:
NDA Dup., Trip.
M-100
M-120
M-300
M-1
M-120/MAWeinberger/snr
10/10/67

Supplement

Vols. 43.1 and 48.2

dated October 10, 1967 and includes the following to the FDA: an introduction and background discussion a summary of the findings in treated patients and individual case reports on treated patients and controls in trigeminal neuralgia and epilepsy and, finally, revised prescribing letter changes were in conformity with suggestions here at FDA attended by Drs. T. P. S. Watts and 2, 1967

and were summarized case by case per investigator and of treated cases (trigeminal neuralgia and epilepsy) In essence, the submission summary consists of raw data of the incidence of the various lesions, that is, the in the treated groups as compared to the control group. referred to Dr. Howard Bernstein who is an ophthalmologist In abnormalities of the eye caused by drugs. analyzed the abnormalities and separated them into the control groups. The data were compiled on 83 patients who trigeminal neuralgia, 52 patients who were treated 91 controls. This makes a total of 226 patients. follows lists the abnormalities encountered and indicates the treated and control groups.

Abnormal Observation	Treated	Controls
1. Hyperemia	7	1
2. Blepharitis	4	0
3. Corneal opacities	9	1
4. Cataracts:		
a. Nuclear sclerosis	19	6
b. Posterior subcapsular	3	1
c. Incipient cataracts	3	0
5. Macular mottling or stippling	7	0
6. Peripheral retinal degeneration	4	1
7. Vascular attenuation or arteriosclerotic changes	7	3

Dr. Bernstein noted that the other observations were either too few in number or equally divided among the control and treated groups. His conclusions were as follows:

1. All observations are consistent with naturally occurring ocular abnormalities. There does not appear to be any abvious qualitatively unique drug-related abnormality.
2. There is a higher incidence of the observations noted under "Results" in the treated group than in the control group and this appears to be higher than the ratio of treated and control patients.

..... however that a graph of the population ps reveals dissimilar age skewed toward the higher age and the younger age groups. in and he agrees that this s that were noted in treated h the higher incidence of older n in a younger age group as cluded that the differences t, but that the type of study done would telon regarding this. He stated that it one a study in which the eye examinations and examinations gan and that these examinations d with a control group.

..... Bernstein's conclusions. The evidence that the drug has induced any ction originally raised by to be resolved.

..... something information as discussed ; plan to recommend some additions lition to be recommended is an first paragraph of the package astic anemia are cited and the ste blood and platelet counts us bone marrow injury early. to augment the description of ngs in the animal studies and be added on therapeutic responses

..... These responses include:

1. Complete symptomatic relief while on the drug.
2. Partial symptomatic relief while on the drug.
3. Complete remission which continued after cessation of drug therapy.
4. Partial or complete symptomatic relief initially with relapse with time.
5. No response.
6. Drug withdrawal because of toxicity.

A meeting has been arranged with the applicant for Wednesday, October 25, 1967 at 2:00 pm and it will be attended by Dr. McKeon and Watts of Geigy and members of the staff of the Division of Neuropharmacologic Drugs.

Morris A. Weinberger

Morris A. Weinberger, M.D.

cc:
NDA Dup., Trip.
M-100
M-120
M-300
M-120/MWeinberger/srw
10/25/67