DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-844

R. W. Johnson Pharmaceutical Research Institute
Attention: Michael H. Kaufman
Associate Director, Regulatory Affairs
920 Route 202 South
P.O. Box 300
Raritan, New Jersey 08869-0602

OCT 2 6 1998

Dear Mr. Kaufman:

Please refer to your new drug application (NDA) dated July 31, 1997, received August 1, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Topamax (topiramate capsules) Sprinkle Capsules 15mg, 25mg, and 50mg.

We acknowledge receipt of your additional correspondence and amendments dated July 21, 1998, and August 26, 1998. Your submission of August 26, 1998 constituted a full response to our July 20, 1998 action letter.

The user fee goal date for this application is October 27, 1998.

This new drug application provides for a sprinkle capsule formulation of topiramate, a new dosage form, as adjunctive therapy for the treatment of adults with partial onset seizures.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the submitted labeling (package insert submitted August 26, 1998, patient package insert submitted August 26, 1998, immediate container and carton labels submitted August 26, 1998) with the revisions listed below. Accordingly, the application is approved effective on the date of this letter.

1. The second sentence of the Oral Contraceptives subsection in the PRECAUTIONS section of the package insert has been revised to the following:

   The mean oral clearance of ethinyl estradiol at 800 mg/day dose was increased by 47% (range: 13- 107%).

   We note that you have agreed to this revision as per the October 7, 1998 telephone conversation between Catherine Glamkowski of R.W. Johnson Pharmaceutical Research Institute and Jacqueline Ware of this Division.

2. References to the 50 mg capsule strength of topiramate have been added to the DESCRIPTION and HOW SUPPLIED sections of the package insert.

   We note that your August 26, 1998 submission advised that references to the 50 mg capsule strength of topiramate were removed from proposed labeling because this strength would not be marketed at this time. However, given that this letter provides an approval action for this application, we are including reference to the 50 mg capsule strength for completeness, It is acceptable to remove reference to the 50 mg capsule strength of topiramate from your final printed labeling.

These revisions are terms of the NDA approval. Marketing the product before making the revisions, exactly as requested, in the product's final printed labeling (FPL) may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 20-844." Approval of this submission by FDA is not required before the labeling is used.

Should additional information relating to the safety and effectiveness of the drug become available, revision of labeling may be required.

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Please submit one market package of the drug product (containers and cartons only) when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact Jacqueline H. Ware, Pharm.D., Regulatory Management Officer, at (301) 594-2850.

Sincerely yours,

/S/ [redacted]

Paul Leber, M.D.
Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research