



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA#s 20-505/S-022 & 20-844/S-019  
NDA#s 20-505/S-025 & 20-844/S-021

The R.W. Johnson  
Pharmaceutical Research Institute  
Attention: Ms. Catherine Glamkowski  
Route 202, P.O. Box 300  
Raritan, NJ 08869-0602

Dear Ms. Glamkowski:

Please refer to your supplemental new drug applications below, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Topamax (topiramate) tablets and sprinkle capsules.

NDA #	Supplement Provides For	Date Submitted
20-505/S-022 & 20-844/S-019	Migraine Prophylaxis	February 13, 2004
20-505/S-025 & 20-844/S-021	Hyperammonemia	April 2, 2004

We acknowledge receipt of your submission dated February 27, 2004.

Your submission of February 13, 2004 constituted a complete response to our October 23, 2003 action letter.

We have completed our review of these applications, as amended. These applications are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert).

In addition, you must submit the content of labeling in electronic format as described in 21 CFR 314.50(1)(5). Current guidance for industry specifies that the content of labeling should be provided in PDF or SPL file format. This new submission requirement was published on December 11, 2003 (68 FR 69009) and was effective June 8, 2004. For additional information, consult the following guidance for industry: *Regulatory Submissions in Electronic Format – Content of Labeling* (February 2004).

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are deferring submission of your pediatric studies for ages 12 to 17 years until August 31, 2007.

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of these postmarketing studies shall be reported annually according to 21 CFR 314.81. This commitment is listed below.

NDA 20-505/S-022 & 20-844/S-019

NDA 20-505/S-025 & 20-844/S-021

Page 2

1. Deferred pediatric study under PREA for the prophylaxis of migraine in pediatric patients ages 12 to 17 years.

Final Report Submission: August 31, 2007

Submit final study reports to this NDA. For administrative purposes, all submissions related to this pediatric postmarketing study commitment must be clearly designated "**Required Pediatric Study Commitments**".

We remind you of your postmarketing commitment in your submission dated August 10, 2004. This commitment is listed below.

We note that you commit to provide a patient package insert (PPI) for the use of Topamax in epilepsy and migraine prophylaxis. We note that you intend to submit a draft PPI no later than November 30, 2004.

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "**Postmarketing Study Protocol**", "**Postmarketing Study Final Report**", or "**Postmarketing Study Correspondence**."

In addition, submit three copies of the introductory promotional materials that you propose to use for these products. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, MD 20857

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410  
FDA  
5600 Fishers Lane  
Rockville, MD 20857

Please submit one market package of the drug product when it is available.

NDA 20-505/S-022 & 20-844/S-019

NDA 20-505/S-025 & 20-844/S-021

Page 3

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Lana Chen, Regulatory Project Manager, at (301) 594-5529.

Sincerely,

*{See appended electronic signature page}*

Russell Katz, M.D.

Director

Division of Neuropharmacological Drug Products

Office of Drug Evaluation I

Center for Drug Evaluation and Research

Enclosure

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**This is a representation of an electronic record that was signed electronically and  
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/s/

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Russell Katz  
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