



NDA 20-505/S-015

NDA 20-844/S-012

Ortho McNeil Pharmaceutical Inc.  
Attention: Catherine M. Glamkowski  
Associate Director, Regulatory Affairs  
1000 Route 202 South, P.O. Box 300  
Raritan, NJ 08869-0602

Dear Ms. Glamkowski:

Please refer to your supplemental new drug applications dated March 25, and received March 26, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Topamax (topiramate) tablets (NDA 20-505) and Topamax (topiramate) sprinkle capsules (NDA 20-844).

We acknowledge receipt of your submission dated April 29, 2003. Your submission of April 29, 2003, constituted a complete response to our March 19, 2003 action letter.

Reference is also made to an electronic communication dated May 13, 2003, from Ms. Tania Hillmer, of your office, to Mr. Paul David, of this Agency, agreeing to revisions to the **OVERDOSAGE** section of product labeling.

These "Prior Approval" supplemental new drug applications propose revisions to the **PRECAUTIONS-Nursing Mothers** and **OVERDOSAGE** sections of product labeling.

We have completed the review of these supplemental applications, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective as submitted in your draft labeling and as revised below. Accordingly, these supplemental applications are approved effective on the date of this letter.

As noted in our March 19, 2003 action letter, we concur with your originally proposed revisions to the **PRECAUTIONS-Nursing Mothers** section of labeling. Additionally, we note your concurrence, as referenced above in your May 13, 2003 communication, to the following revisions to the **OVERDOSAGE** section of labeling:

#### **OVERDOSAGE**

Overdoses of Topamax have been reported. Signs and symptoms included convulsions, drowsiness, speech disturbance, blurred vision, diplopia, mentation impaired, lethargy, metabolic acidosis, abnormal coordination, stupor, hypotension, abdominal pain, agitation, dizziness, and depression. The clinical consequences were not severe in most cases, but deaths have been reported after poly-drug overdoses involving Topamax.

A patient who ingested a dose between 96 and 110 g topiramate was admitted to hospital with coma lasting 20-24 hours followed by full recovery after 3 to 4 days.

In acute Topamax overdose, if the ingestion is recent, the stomach should be emptied immediately by lavage or by induction of emesis. Activated charcoal has been shown to adsorb topiramate *in vitro*. Treatment should be appropriately supportive. Hemodialysis is an effective means of removing topiramate from the body.

Please submit the copies of final printed labeling (FPL) electronically to each application according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no 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, these submissions should be designated "FPL for approved supplements 20-505/S-015 & 20-844/S-012" Approval of these submissions by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2  
FDA  
5600 Fishers Lane  
Rockville, MD 20857

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 regarding this letter, call Paul David, R.Ph., Senior Regulatory Project Manager, at (301) 594-5530.

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

-----  
**This is a representation of an electronic record that was signed electronically and  
this page is the manifestation of the electronic signature.**  
-----

/s/

-----  
Russell Katz

6/3/03 08:28:24 AM