DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-505/S-020
NDA 20-844/S-017

Ortho-McNeil Pharmaceutical, Inc.
c/o Johnson & Johnson Pharmaceutical Research & Development, L.L.C.
Attention: Catherine M. Glamkowski
920 Route 202 South, P.O. Box 300
Raritan, New Jersey 08869-0602

Dear Ms. Glamkowski:

Please refer to your supplemental new drug applications dated December 11, 2002, received December 12, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Topamax (topiramate) Tablets and Topamax (topiramate capsules) Sprinkle Capsules.

These "Changes Being Effected" supplemental new drug applications provide for the addition of information to the WARNINGS and PRECAUTIONS/Information for Patients sections of the Topamax package insert regarding oligohidrosis.

We acknowledge receipt of your submissions dated March 12, 2003 in which you accepted the Division's January 31, 2003 proposed revisions to the oligohidrosis language in the WARNINGS and PRECAUTIONS/Information for Patients sections of Topamax labeling.

Reference is also made to the May 21, 2003 teleconference between representatives of Johnson & Johnson Pharmaceutical Research & Development and this Division. During this teleconference, it was agreed that the agreed-upon revisions of the oligohidrosis language for Topamax labeling would appear as a non-bolded statement in the WARNINGS section.

We have completed our review of these supplemental applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug products are 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.

We note your concurrence, as referred to in the above communications, that the following new statements are to be added to the WARNINGS and PRECAUTIONS/ Information for Patients sections of labeling:

WARNINGS
Oligohidrosis and Hyperthermia: Oligohidrosis (decreased sweating), infrequently resulting in hospitalization, has been reported in association with Topamax use. Decreased sweating and an elevation in body temperature above normal characterized these cases. Some of the cases were reported after exposure to elevated environmental temperatures.

The majority of the reports have been in children. Patients, especially pediatric patients, treated with Topamax should be monitored closely for evidence of decreased sweating and increased body temperature, especially in hot weather. Caution should be used when Topamax is prescribed with other drugs that predispose patients to heat- related disorders; these drugs include, but are not limited to, other carbonic anhydrase inhibitors and drugs with anticholinergic activity.

PRECAUTIONS/ Information for Patients
Patients, especially pediatric patients, treated with Topamax should be monitored closely for evidence of decreased sweating and increased body temperature, especially in hot weather.

Please submit the FPL electronically according to the guidance for industry titled "Providing Regulatory Submissions in Electronic Format – NDA". Alternatively, you may submit 20 paper 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 heavyweight paper or similar material. For administrative purposes, these submissions should be designated "FPL for approved supplements NDA 20-505/S-020 and NDA 20-844/S-017." Approval of these submissions by FDA is not required before the labeling is used.

Lastly, we note your agreement, during our May 21, 2003 teleconference, to issue a letter communicating this important safety information about these drug products (i.e., a "Dear Health Care Professional" letter) and request that you submit a copy of the letter to these NDAs and a copy to the following address:

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

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 Jacqueline H. Ware, Pharm.D., Senior Regulatory Project Manager, at (301) 594-2850.

Sincerely,

{See appended electronic signature page}

Russell Katz, M.D.
Director
Division of Neuropharmacological Drug Products
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

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