DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-299/S-013

Synthon Pharmaceuticals, Ltd.
Attention: Kamali Chance, MPN, Ph.D., RAC
Director of Regulatory Affairs
6330 Quadrangle Drive, Suite 205
Chapel Hill, NC 27517

Dear Dr. Chance:

We acknowledge receipt of your supplemental new drug application dated November 12, 2004, and received November 15, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Pexeva [paroxetine (as mesylate)] Tablets, 10 mg, 20 mg, 30 mg and 40 mg.

Reference is also made to an Agency letter dated October 15, 2004, requesting class labeling changes for all of the drugs approved to treat major depressive disorder (MDD) to caution practitioners, patients, family members or caregivers about an increased risk of suicidal thinking and behavior (suicidality) in children and adolescents with MDD and other psychiatric disorders who are taking antidepressant medications.

We additionally refer to an e-mail from Mr. Paul David, of this Division, sent to you on October 21, 2004, providing you with a draft Medication Guide and instructions that a Medication Guide should be submitted to FDA in conjunction with the prescriber labeling changes as requested in our October 15, 2004 letter.

Finally, reference is made to an e-mail communication dated October 27, 2004, from Mr. Paul David, informing you that the supplement, consisting of the prescriber labeling revisions as well as the addition of the Medication Guide, should be submitted as a "Prior Approval" supplement, and that we were soliciting feedback from the various sponsors on the class prescriber labeling as well as the class Medication Guide prior to final implementation by the sponsors.

This supplement provides for the addition of a boxed warning and other changes to product labeling and the addition of a Medication Guide pertaining to pediatric suicidality.

We have completed our review of your application as well as the various sponsors' labeling and Medication Guide counterproposals sent in response to the requests. The final approved labeling and Medication Guide are attached to this letter. There may be slight differences between your proposed labeling and the final labeling we have attached, but we regard the deficiencies in your proposed label as minor within the meaning of 21 CFR 314.105(b). Accordingly, this application is approved with the attached labeling effective on the date of this letter.

You should submit final printed labeling (FPL) identical to the enclosed labeling (text for the package insert and Medication Guide). For administrative purposes, this submission should be designated "FPL for approved supplement 21-299/S-013." Also, you should provide a date when the labeling will be available

on your products. Since we have developed standardized labeling for all antidepressants used in children because of safety concerns associated with the use of these products in children, final printed labeling should be available on your WEB page within two weeks of the date of this letter, and on all products within 30 days. Failure to make these changes within the specified period of time could make your product misbranded under 21 USC 321(n) and 352(a).

Regarding the Medication Guide, the free-standing Medication Guide must be exactly as in the attached document, with no mention of any specific drugs or the sponsor. Although the ultimate goal is to have the Medication Guide attached to unit-of-use packaging, until such packaging becomes available, it is our expectation that you will prepare tear-off pads or provide for some other means of disseminating these standard antidepressant Medication Guides and make such tear-offs or means available to pharmacists and physicians by January 31, 2005.

(b)(4)

In addition, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed the revised labeling and has determined that it contains significant new risk information relating to your drug product. DDMAC is hereby informing you that all promotional materials for your drug product that include representations about your drug product should be revised to include the new risk information no later than 30 days from the date of this letter. These revisions should include prominent disclosure of the information from the new boxed warning and warning sections that appear in the revised package insert. If you have any questions about the promotion of your drug products, please contact the Food and Drug Administration, Division of Drug Marketing, Advertising, and Communications by facsimile at (301) 594-6771 or at HFD-42, Room 8B-45, 5600 Fishers Lane, Rockville, MD 20857.

If you have any other questions, 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

Attachments (2)

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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