CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 18-936/S-060/S-062/S-063

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 18-936/S-060/S-062/S-063

NOV 28 2000

Eli Lilly and Company
Attention: Gregory T. Brophy, Ph.D.
Director, U.S. Regulatory Affairs
Lilly Corporate Center
Indianapolis, IN 46285-2643

Dear Dr. Brophy:

Please refer to your supplemental new drug applications dated July 6, 1999 (S-060), August 22, 2000 (S-062), and August 31, 2000 (S-063) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prozac (fluoxetine hydrochloride) pulvules to treat depression, obsessive compulsive disorder (OCD), and bulimia nervosa and Sarafem (fluoxetine hydrochloride) pulvules to treat premenstrual dysphoric disorder (PMDD).

Reference is also made to an Agency approvable letter dated May 2, 2000, for S-060, and to a telephone conversation between Mr. Paul David of this Agency and David Johnson of your firm dated July 6, 2000, agreeing on labeling revisions to the Sarafem labeling.

We additionally acknowledge receipt of your submission dated November 8, 2000, providing for revisions to your proposed labeling as requested by the Agency.

These supplemental new drug applications provide for the following revisions to the Prozac and Sarafem product labeling:

S-060

This supplemental application provides for revisions to the **ADVERSE REACTIONS-Other Events Observed in US Clinical Trials**, and **ADVERSE REACTIONS-Postintroduction Reports**

S-062

This supplemental application provides for a harmonization of the Prozac labeling with the approved labeling for Sarafem, the fluoxetine drug product for the treatment of PMDD. Specifically, these changes provide for the following revisions:

1. A cautionary statement in the **DESCRIPTIONS** section of labeling that Sarafem is the same product as Prozac.
2. A statement that thioridazine should not be used with Prozac in the **CONTRAINDICATIONS, WARNINGS**, and **PRECAUTIONS** sections of labeling.
3. The addition of two additional adverse event terms of "lupus-like syndrome" and "laryngospasm" into the **WARNINGS** section.

4. An addition of a subsection entitled **Sumatriptan** under **PRECAUTIONS-Drug Interactions** section.
5. The addition of a subsection entitled **Male and Female Sexual Dysfunction with SSRIs** under the **ADVERSE REACTIONS** section.
6. The addition of several terms to the **ADVERSE REACTIONS-Postintroduction Reports** section.
7. A complete revision of the **OVERDOSAGE** section.
8. An addition to the **HOW SUPPLIED** section of a "Protect from light" statement. We additionally remind you of your commitment, previously communicated to you in an Agency letter dated July 6, 2000, to monitor the drug product in photostability studies, to submit the results of such studies before January 6, 2001, and to remove the light protection instruction from labeling via a CBE-30 supplement if the stability studies demonstrate that light protection is not necessary.

S-063

This supplemental application provides for final printed labeling as requested in the Agency approval letter dated July 6, 2000, providing for the approval of fluoxetine, under the tradename of Sarafem, for PMDD. The revisions to the labeling also incorporated changes that were agreed upon in the aforementioned telephone conversation dated July 6, 2000.

We have completed the review of these supplemental applications, 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 agreed upon labeling text. Accordingly, these supplemental applications are approved effective on the date of this letter.

Labeling changes of the kind which you have proposed under S-063 are permitted by section 314.70(c) of the regulations to be instituted prior to approval of the supplement. It is understood that the changes, described in the above NDA supplement 063, have been made.

We note that supplemental applications 060 and 062 were submitted under changes requiring prior approval. The final printed labeling (FPL) of these supplements must be identical to the submitted draft labeling (package insert submitted November 8, 2000).

Please submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed to each application. Please individually mount ten of the copies on heavy-weight paper or similar material. Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999). For administrative purposes, these submissions should be designated "FPL for approved supplement NDA 18-936/S-060, S-062." 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, call Paul David, R.Ph., Regulatory Project Manager, at (301) 594-5530.

Sincerely,

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