



NDA 20-936

SmithKline Beecham Pharmaceuticals
Attention: Thomas F. Kline
Manager, U.S. Regulatory Affairs
1250 South Collegeville Road, P.O. Box 5089
Collegeville, Pennsylvania 19426

Dear Mr. Kline:

Please refer to your New Drug Application dated and received December 19, 1997, submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for Paxil CR (paroxetine hydrochloride) Controlled-Release 12.5 mg and 25 mg Tablets.

Reference is also made to an Agency approvable letter dated October 9, 1998, and to your submissions dated November 19, 1998, December 18, 1998, January 11, 1999, and January 25, 1999.

This new drug application provides for the use of Paxil CR for the treatment of depression.

We have completed the review of this application, 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 enclosed labeling text. Accordingly, the application is approved effective on the date of this letter.

Accompanying this letter (ATTACHMENT) is the labeling, including the revisions agreed to in a conversation dated February 4, 1999 between yourself and Mr. Paul David of this Agency, that should be used for marketing this drug product. These revisions are terms of the NDA approval. Marketing the product before making the agreed upon revisions in the product's labeling may render the product misbranded and an unapproved new drug.

We have the following additional comments:

MANUFACTURING AND CONTROLS

1. Expiration Date

The available stability data at the present time support an expiry date not to exceed 18 months for the 12.5 mg and 25 mg tablet strengths.

2. Manufacturing Sites

Please note that you are only approved to manufacture drug product at your Crawley, UK facility at this time.

3. Methods Validation

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

BIOPHARMACEUTICS

We note your agreement to the following dissolution method and specification for both strengths of Paxil CR Tablets (12.5 mg and 25 mg):

Apparatus: USP II (paddles) 150 rpm

Dissolution Media	Time	Limit (% dissolved)
Step 1: 0.1 M HCL (750 mL) for 2 hours	2 hours	Not more than (b)
Step 2: pH 7.5 Tris buffer containing 60 mmol Tris, 90 mmol NaCl (1000 mL) for 7 hours	1 hour	(b)(4)(
	2 hours	CC)-----
	4 hours	-----
	6 hours	-----

The final printed labeling (FPL) must be identical to the enclosed labeling. Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 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 heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 20-936." Approval of this submission by FDA is not required before the labeling is used.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit 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-40
 Food and Drug Administration
 5600 Fishers Lane
 Rockville, Maryland 20857

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

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, contact Paul David, R.Ph., Regulatory Project Manager, at (301) 594-5530.

Sincerely,

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

ATTACHMENT