CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

NDA 20-710/S-002

Name:	Paxil Tablets and Oral Suspension
Generic:	paroxetine hydrochloride
Sponsor:	GlaxoSmithKline
Approval Date:	02/20/1998

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-710/S-002

CONTENTS

Reviews / Information Included in this Review	
Approval Letter	X
Approvable Letter(s)	
Final Printed Labeling	
Medical Review(s)	
Chemistry Review(s)	X
EA/FONSI	
Pharmacology Review(s)	
Statistical Review(s)	
Microbiology Review(s)	
Clinical Pharmacology/Biopharmaceutics Review(s)	
Administrative and Correspondence Document(s)	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-710/S-002

APPROVAL LETTER

NDA 20-710/S-002

FEB 20 1998

SmithKline Beecham Pharmaceuticals
Attn: David Korman
1250 South Collegeville Road
P.O. Box 5089
Collegeville, PA 19426-0989

Dear Mr. Korman:

Please refer to your supplemental new drug application dated January 29, 1998, received January 30, 1998 submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetics Act for Paxil® (paroxetine hydrochloride) Oral Suspension.

The User Fee goal date for this application is July 29, 1998.

This supplemental application provides for the optional use of [ ] Stage / material directly into the Stage / process, bypassing the currently approved [ ] of the Stage / material. The supplement was submitted as "Special Supplement - Changes Being Effected."

We have completed the review of this supplemental new drug application and it is approved.

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, please contact Mr. Paul David, Regulatory Project Management Officer, at (301) 594-2850.

Sincerely,

Maryla Guzewska, Ph.D.
Chemistry Team Leader (acting), DNDC-1
Division of Neuropharmacological Drug Products
(HFD-120)
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc: Original NDA 20-710
HFD-120/Div. Files
HFD-120/PDavid
HFD-120/MZarifa
HFD-120/MGuzewska mg 2.19.98
HFD-92/DDM-DIAB
HFR-MA100/Phil-DO

Drafted by: MZarifa
Initialed by: MGuzewska

APPROVED

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-710/S-002

CHEMISTRY REVIEW(S)

FEB 19 1998

CHEMIST REVIEW OF SUPPLEMENT

1. ORGANIZATION: **HFD-120**

2. NDA NUMBER: ***20-710***

4. SUPPLEMENT NUMBERS/DATES: **S-02**

LETTERDATE 27-JAN-98

STAMPDATE 30-JAN-98

5. AMENDMENTS/REPORTS/DATES:

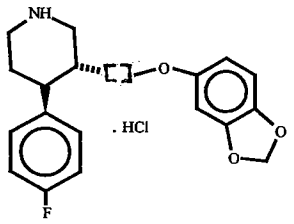
LETTERDATE

STAMPDATE

6. REC'D BY CHM: 03-FEB-98

7. APPLICANT NAME AND ADDRESS:

SmithKline Beecham
Pharmaceuticals
Four Falls Corporate Center
Route 23 & Woodmont Avenue
P.O.Box 1510
King of Prussia, PA 19406



8. NAME OF DRUG: **Paxil®**

9. NONPROPRIETARY NAME: Paroxetine hydrochloride

10. CHEMICAL NAME/STRUCTURE: (-)trans-4R-(4'-Fluorophenyl)-3S-[3',4'methylene-dioxphenoxy)methyl]piperidine hydrochloride hemihydrate

11. DOSAGE FORM(S): Oral suspension

12. POTENCY(IES): 10 mg/5 mL

13. PHARM. CATEGORY: Depression

14. HOW DISPENSED: **XXX (Rx) ___ (OTC)**

15. RECORDS AND REPORTS CURRENT: **XXX (YES) ___ (NO)**

16. RELATED IND/NDA/DMF(S):

17. SUPPLEMENT PROVIDES FOR: Modifications in the manufacturing process and controls of the drug substance.

18. COMMENTS: SKB is proposing the optional use of step / intermediate as the [ ] intermediate without passing through the approved [ ] step. The change is introduced as a Change Being Effected (CBE). SKB provides an adequate description of the modified process and comparative batch analyses results for the drug substance to demonstrate that the [ ] intermediate produces an acceptable intermediate in step / of the synthesis and no change in [ ] material. The CMC review was done by HFD-110. **See CMC Review Notes of HFD-110 for details.**

19. CONCLUSIONS AND RECOMMENDATIONS: Changes Being Effected are acceptable. Recommend APPROVAL of NDA 20-031 Supplement 22. An inspection request for this CBE supplement is not needed.

20. REVIEWER NAME	***SIGNATURE***	***DATE COMPLETED***
Mona Zarifa, Ph.D.	Mona Zarifa	**February 18, 1998**

Copies:
ORIG. NDA
HFD-120
HFD-120/PDavid
HFD-120/MZarifa/

Filename: **20710002.000**

INIT: **MG/** 2.19.98

Redacted 3 page(s)

of trade secret and/or

confidential commercial

information from

Chemistry Review

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-710/S-002

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-710/S-002

SMITHKLINE BEECHAM
1250 S. COLLEGEVILLE ROAD
P.O. BOX 5089
COLLEGEVILLE, PA 19426

FEB 6 1998

Attention: DAVID KORMAN

Dear: MR. KORMAN

We acknowledge receipt of your supplemental application for the following:

Name of Drug: PAXIL ORAL SUSPENSION

NDA Number: 20-710

Supplement Number: S-002

Date of Supplement: JANUARY 29, 1998

Date of Receipt: JANUARY 30, 1998

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on MARCH 31, 1998 in accordance with 21 CFR 314.101(a).

All communications concerning this NDA should be addressed as follows:

Center for Drug Evaluation and Research
Division of Neuropharmacological Drug Products, HFD-120
Office of Drug Evaluation I
Attention: Document Control Room 4008
5600 Fishers Lane
Rockville, MD 20857

Sincerely,

John S. Purvis
Chief, Project Management Staff
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc:
Original NDA 20-710/002
HFD-120/Div. Files
HFD-120/CSO/PAUL DAVID

filename:

SUPPLEMENT ACKNOWLEDGEMENT

SmithKline Beecham
Pharmaceuticals

ORIGINAL

January 29, 1998

NDA NO. 20-710 REF. NO. SS-002
NOT USED FOR Control

CENTER FOR DRUG EVALUATION AND RESEARCH

JAN 30 1998

RECEIVED HFD-120

NDA 20-710
Paxil® (paroxetine hydrochloride) Oral Suspension

Paul Leber, M.D., Director
Division of Neuropharmacological
Drug Products (HFN-120, Room 10B-45)
Center for Drug Evaluation and Research
Office of Drug Evaluation I
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Re: Special Supplement "Changes Being Effected"

Dear Dr. Leber:

Reference is made to NDA 20-710, Paxil® (paroxetine hydrochloride) Oral Suspension. Further reference is made to paroxetine hydrochloride stages [ ] through [ ], which are performed at the SB Cork facility. Provided herewith is information in support of a minor processing change, allowing for the optional use of [ ] stage / material directly into the stage / process, bypassing the currently approved [ ] of the stage / material. This change was submitted to NDA 20-031, Paxil® (paroxetine hydrochloride) Tablets as a "SS-CBE" on January 21, 1998.

Currently, each of the stages is [ ] prior to use in the following stage and must meet an assay specification on an "as is" basis. Upon implementation of the proposed change, the [ ] stage / material would be required to meet the identical assay specification, which would be measured on a [ ] basis. The only change to the stage / specification is to account for analysis of [ ] material (see appendix 2).

To evaluate the proposed change, three trial plant batches of paroxetine stage / material were manufactured using [ ] paroxetine stage / material. The quality of the material at stages [ ] was determined (versus specification), and the change has been evaluated based on the quality of the stage / material.

000001

Y:\PAXIL\20-710\SSORAL.DOC\1

Results

Four plant batches of paroxetine stage / material at 100% batch size were manufactured under normal processing conditions, but were not [ ]. The assay was measured on a [ ] basis (see appendix 3 - method modification to incorporate an LOD test and to stipulate testing on LOD material). All four batches met stage / specification and the results were within the normal range for production scale batches. Batch analysis data is contained in Table 2.

Six plant batches of paroxetine stage / material at 100% batch size were manufactured under normal processing conditions using the [ ] stage / material. All six batches met stage / specifications and the results were within the normal range for production scale batches. Batch analysis data is contained in Table 3.

Three plant batches of paroxetine stage / material (two at 75% batch size, one at 50% batch size) were manufactured using normal processing conditions. All three batches met stage / specification, and the results were within the normal range for production scale batches. Batch analysis data is contained in Table 4.

Stability of [ ] Paroxetine Stage /

All four batches of [ ] Paroxetine stage / material were held under normal storage conditions for 18 weeks prior to processing to stage /
A stability program has been established to cover intended storage period for [ ] [ ] Paroxetine stage / material. Stability samples will be analyzed at 0,1,3,6 and 9 month timepoints.

These changes are effective immediately.

If you have any questions regarding this submission, please contact the undersigned at (610) 917-5638.

Sincerely,

David Korman

David Korman
Senior Associate
Regulatory Affairs, North America