CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
NDA 20-031/S-028

Name:	Paxil Tablets (paroxetine hydrochloride)
Sponsor:	SmithKline Beecham Pharmaceuticals
Approval Date:	September 21, 2000

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-031/S-028

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 Document(s)	
Correspondence Document(s)	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-031/S-028

APPROVAL LETTER

114.1

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville MD 20857

NDA 20-031/S-028
NDA 20-710/S006
NDA 20-885/S-001
NDA 20-936/S-003

SEP 21 2000

SmithKline Beecham
Attention: Ms. Deborah Zuber
Assistant Director, US Regulatory Affairs
1250 South Collegeville Road
P.O. Box 5089
Collegeville, PA 19426-0989

Dear Ms. Zuber:

Please refer to your supplemental new drug applications dated June 26, 2000, received June 29, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Paxil Hydrochloride.

These supplemental new drug applications provide updated information pertaining to changes in the synthesis of paroxetine hydrochloride since the 1999 and 2000 annual reports.

We have completed the review of these supplemental applications, and they are 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, call Paul David, R.Ph., Regulatory Project Manager, at (301) 594-5530.

Sincerely,

9/22/00

Robert H. Seevers, Ph.D.
Chemistry Team Leader, Psychiatric Drugs for the
Division of Neuropharmacological Drug Products,
(HFD-120)
DNDC I, Office of New Drug Chemistry
Center for Drug Evaluation and Research

cc:
Archival NDAs 20-031, 20-710, 20-885, 20-936
HFD-120/Div. Files
HFD-120/P.David
HFD-120/S.McLamore
HFD-120/R.Seevers
HFD-095/DDMS-IMT
HFD-093/DDMS-IST (with labeling)
HFD-810/DNDC Division Director
DISTRICT OFFICE

Drafted by: sdm/September 14, 2000
Initialed by:
final:
filename: 20031

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-031/S-028

CHEMISTRY REVIEW(S)

SEP 21 2000

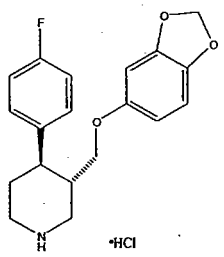
CHEMIST REVIEW
OF **SUPPLEMENT**

1. **ORGANIZATION:** HFD-120
2. **NDA** [redacted]
20-710 SCS-006
20-885 SCS-001
20-936 SCS-003

3. **SUPPLEMENT DATES:**
LETTER DATE: 06-26-00
STAMP DATE: 06-29-00
4. **AMENDMENT/REPORTS/DATES**
5. **RECEIVED BY CHEMIST:** 07-07-00

6. **APPLICANT NAME & ADDRESS:** SmithKline Beecham Pharmaceuticals
1250 South Collegeville Road
P.O. Box 5089
Collegeville, PA 19426-0989

7. **NAME OF DRUG:** Paxil
8. **NONPROPRIETARY NAME:** Paroxetine Hydrochloride
9. **CHEMICAL NAME and STRUCTURE:**
(-) trans-4*R*-(4′-fluorophenyl)3*S*-[(3′, 4′-methyllenedioxyphenoxy) methyl] piperidine hydrochloride hemihydrate



10. **DOSAGE FORMS:**
NDA 20-031 Tablets
NDA 20-710 Oral Suspension
NDA 20-885 Capsules
NDA 20-936 CR Tablets

11. **POTENCY:**
NDA 20-031 10, 20, 30 and 40 mg
NDA 20-710 10 mg
NDA 20-885 10, 20, 30 and 40 mg
NDA 20-936 12.5 and 25 mg

12. **PHARMACOLOGICAL CATEGORY:** Antidepressant
13. **HOW DISPENSED:** X R(x) _____ (OTC)
14. **RECORD and REPORTS CURRENT:** X Yes _____ No
15. **RELATED IND/NDA/DMF:** DMF 14475

16. **SUPPLEMENT PROVIDES FOR:** These prior approval supplements provide updated information pertaining to changes in the synthesis of paroxetine hydrochloride hemihydrate since the annual reports of February 26, 1999 and February 28, 2000. All information included in this submission has been formally submitted to DMF 14475. The applicant includes copies of the sections of DMF 14475 which contains many the changes that are noted in this submission. The changes contained in these applications include:

- [redacted]
- [redacted]

17. **ADDITIONAL COMMENTS:** The applicant references either DMF 14475, the February 1999 and February 2000 annual report for each of the changes sited in the applications. The changes are all minor with the exception of a [ ] step at stage [ ]. The applicant included a complete description of the process and includes analytical results as well as 9 months of stability data.

18. **CONCLUSIONS & RECOMMENDATIONS:** The sponsor has submitted adequate information to support the changes included in this supplement. It is the recommendation of the CMC reviewer that these supplements be **APPROVED.**

Sherita D. McLamore, Ph.D. (Review Chemist) — Date: 9-21-00

Robert Seevers, Ph.D. (Team Leader) — Date: 9/21/00

cc:
Division File NDA 20-031
Division File NDA 20-936
Division File NDA 20-885
Division File NDA 20-710
HFD-120/RSeevers
HFD-120/SMcLamore
HFD-120/PDavid

Redacted 5 page(s)

of trade secret and/or

confidential commercial

information from

Chemistry Review

5-028

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-031/S-028

CORRESPONDENCE

Food and Drug Administration
Rockville MD 20857

NDA 20-031/S-028

JUL - 7 2000

SmithKline Beecham Pharmaceuticals
1250 Collegeville Road
P.O. Box 5089
Collegeville, PA 19426-0989

Attention: Deborah Zuber
Assistant Director U.S. Regulatory Affairs

Dear Ms. Zuber :

We acknowledge receipt of your supplemental application for the following:

Name of Drug: Paxil Tablets

NDA Number: 20-031

Supplement Number: 028

Date of Supplement: 26-Jun-00

Date of Receipt: 29-Jun-00

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on 28-Aug-2000 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,

7/7/00

John S. Purvis
Chief, Project Management Staff
Division of Neuropharmacological Drug Products, HFD-120
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc:
Original NDA 20-031/028
HFD-120/Div. Files
HFD-120/CSO/David

filename:

SUPPLEMENT ACKNOWLEDGEMENT

ORIGINAL

SmithKline Beecham
Pharmaceuticals

NDA SUPPLEMENT

CENTER FOR DRUG EVALUATION AND RESEARCH

JUN 29 2000

NDA NO. 20-031 REF NO. SCS-028
NDA SUPPL FOR Controls

June 26, 2000 RECEIVED HFD-120

NDA 20-031
Paxil® (paroxetine hydrochloride hemihydrate) Tablets, 10 mg, 20 mg, 30 mg and 40 mg
NDA 20-710
Paxil® (paroxetine hydrochloride hemihydrate) Oral Suspension
NDA 20-885
Paxil® (paroxetine hydrochloride hemihydrate) Capsules, 10 mg, 20 mg, 30 mg and 40 mg
NDA 20-936
Paxil® (paroxetine hydrochloride hemihydrate) CR Tablets, 12.5 mg and 25 mg

Russell Katz, M.D., Director
Food and Drug Administration
Division of Neuropharmacological
Drug Products, Room 4037
1451 Rockville Pike
Woodmont 2
Rockville, Maryland 20852

RE: Prior Approval Supplement - DMF #14475, Updated Chemistry, Manufacturing and Controls Changes

Dear Dr. Katz:

Reference is made to the following SmithKline Beecham Pharmaceuticals' approved New Drug Applications:

- NDA 20-031, Paxil® (paroxetine hydrochloride hemihydrate) Tablets, 10 mg, 20 mg, 30 mg and 40 mg, (submitted November 20, 1989, approved December 29, 1992)

- NDA 20-710, Paxil® (paroxetine hydrochloride hemihydrate) Oral Suspension, (submitted April 2, 1996, approved June 25, 1997)

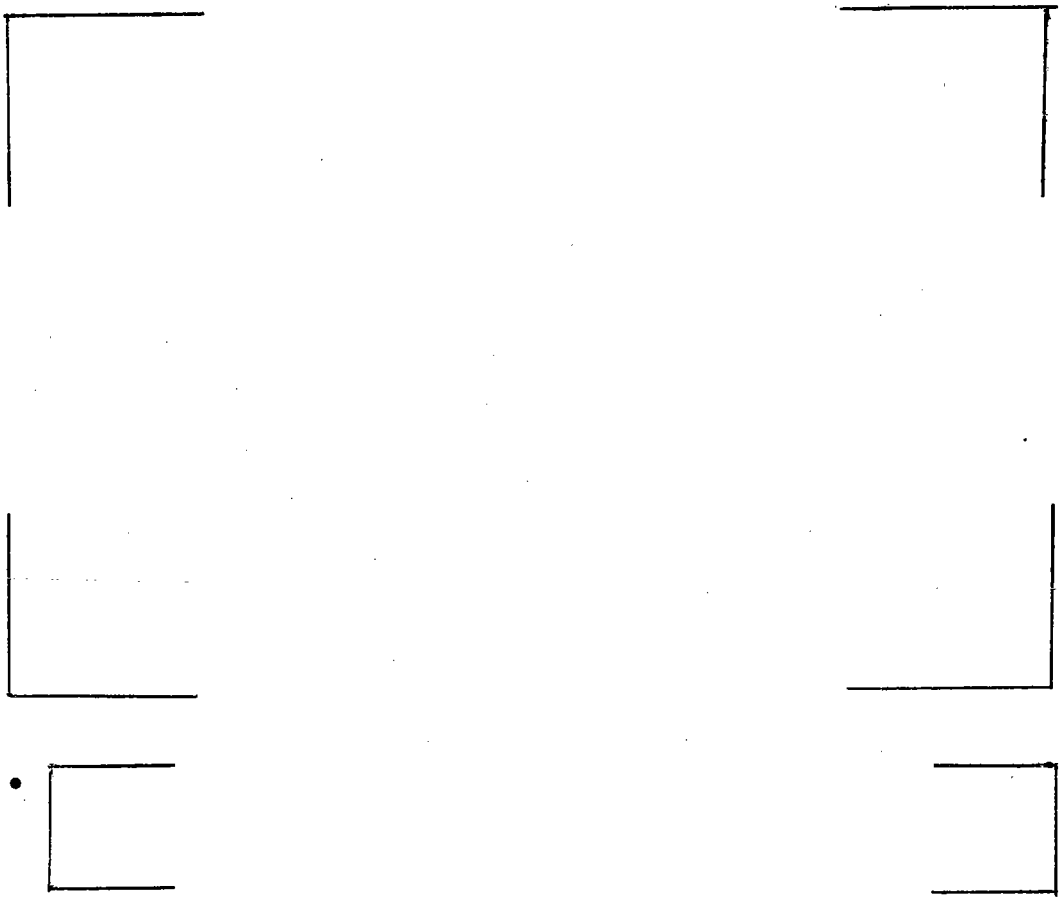
- NDA 20-885, Paxil® (paroxetine hydrochloride hemihydrate) Capsules, 10 mg, 20 mg, 30 mg and 40 mg, (submitted December 22, 1997, approved October 9, 1998)

F:\Paxil\PAtoPaxil\1

1250 S. Collegeville Road, PO Box 5089, Collegeville, PA 19426-0989. Telephone (610) 917 7000. Fax (610) 917 7707.

- NDA 20-936, Paxil® (paroxetine hydrochloride hemihydrate) CR Tablets, 12.5 mg and 25 mg, (submitted December 19, 1997, approved February 16, 1999)

Reference is also made to the drug substance C/M/C information contained in the above-referenced NDAs. Specifically, details of the synthesis of paroxetine hydrochloride hemihydrate are found in the Paxil® (paroxetine hydrochloride hemihydrate) Tablets, NDA 20-031. Further reference is made to the Paxil® (paroxetine hydrochloride hemihydrate) Tablets, NDA 20-031 Annual Reports of February 26, 1999 and February 28, 2000 wherein C/M/C updates were provided to these files.



Redacted 2 page(s)

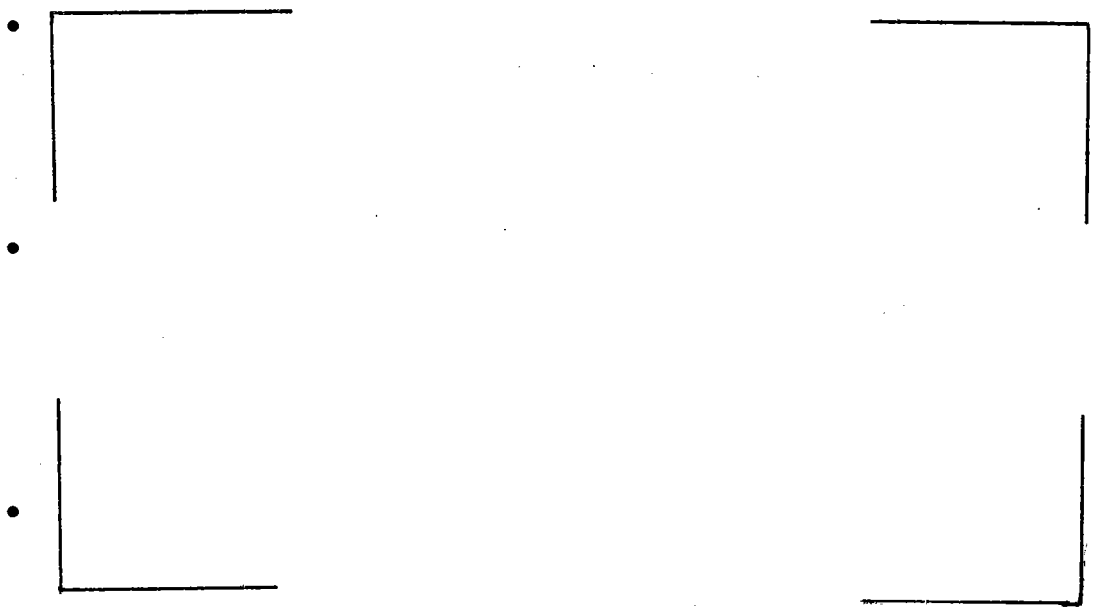
of trade secret and/or

confidential commercial

information from

Correspondence (Re: Prior Approval Supplement.. - 6/26/00)

5-028



We trust the agency will find this submission satisfactory; however, if there are any questions, please do not hesitate to contact me at (610) 917-6884.

Sincerely,

Lynn Kruger for

Deborah Zuber
Assistant Director
U.S. Regulatory Affairs

cc: District Office Copies:
NDA 20-031 - Maridalia Torres, San Juan District Office (full copy)
Debra Pagano, Philadelphia District Office (cover letter)
NDA 20-710- Rochelle Kimmel, DEIO (full copy)
Debra Pagano, Philadelphia District Office (cover letter)
NDA 20-885 - Rochelle Kimmel, DEIO (full copy)
Debra Pagano, Philadelphia District Office (cover letter)
NDA 20-936 - Rochelle Kimmel, DEIO (full copy)
Debra Pagano, Philadelphia District Office (cover letter)

F:\Paxil\PAtoPaxil\5