CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

20-936/S007
20-031/S034
20-710/S011
20-885/S004

Trade Name: Paxil CR
Paxil Tablets
Paxil Capsules
Paxil Oral Suspension

Generic Name: (paroxetine hydrochloride)

Sponsor: SmithKline Beecham Pharmaceuticals

Approval Date: April 30, 2001

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
20-936/S007
20-031/S034
20-710/S011
20-885/S004

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-936/S007
20-031/S034
20-710/S011
20-885/S004

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-031/SCM034, 20-710/SCM-011, 20-885/SCM004, 20-936/SCM007

SmithKline Beecham Pharmaceuticals
Attention: Deborah E. Zuber
Assistant Director, US Regulatory Affairs
1250 South Collegeville Road, PO Box 4089
Collegeville, PA 19426-0989

Dear Ms. Zuber:

Please refer to your supplemental new drug application dated December 29, 2000 received January 3, 2001 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Paxil® Tablets, Paxil® Capsules, Paxil® CR Tablets, Paxil® Oral Suspension.

We acknowledge receipt of your submissions dated February 16 and April 20, 2001.

These supplemental new drug applications provide for use of an alternate modified route of manufacture (b) (4) of Paroxetine HCl using (b) (4) method. The changes in manufacture affect DMF's 15039 and 14475 for Paroxetine HCl (b) (4)

We have completed the review of these supplemental applications, and they are approved with the following comments.

1. **We acknowledge your agreement to monitor the first (b) (4) validation batches manufactured using the (b) (4) at Cork, Ireland and Irvine, Scotland for the (b) (4) at (b) (4) at the respective manufacturing sites. If any (b) (4) is detected a (b) (4) in any batch using (b) (4) method, GlaxoSmithKline is required to report the results to FDA immediately for appropriate action.**

2. **We recommend that for all future submissions for these and other NDA's use only a GMP approved site (b) (4) support of an NDA and post-approval manufacturing changes (b) (4) (b) (4)**

We remind you of your postmarketing commitment in your submission dated April 20, 2001. The commitment is listed below.

1. **We acknowledge your commitment to analyze the batch data obtained from the first (b) (4) months of production using (b) (4) at the Cork, Ireland and Irvine, Scotland facilities and propose tightening of specifications for the (b) (4) Please note that this submission is a Prior Approval supplement to be filed within 12 months of the date of this letter after the first (b) (4) months of production of Paroxetine HCl**

using the (b) (4) **method.**

Study Start: With commercial production of Paroxetine HCl with (b) (4) method.
Final Report Submission: Within 12 months of the date of this letter

In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to these NDAs. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled **"Postmarketing Study Protocol", "Postmarketing Study Final Report", or "Postmarketing Study Correspondence."**

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,

{See appended electronic signature page}

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 NDA 20-031/20-710/20-885/20-936
HFD-120/Div. Files
HFD-120/GGill-Sangha
HFD-120/RSeevers
HFD-120/PDavid
HFD-095/DDMS-IMT
HFD-810/DNDC Division Director
DISTRICT OFFICE

Drafted by: ggs/April 26, 2001
filename: C:/data/My Documents/data gill/Supplement NDA/20-031-710-885-93/
AP-34-11-7-4LTR.doc

APPROVAL (AP)

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Robert H. Seevers
4/30/01 12:19:12 PM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-936/S007

20-031/S034

20-710/S011

20-885/S004

OTHER ACTION LETTER(s)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-031/SCM034
NDA 20-885/SCM004
NDA 20-936/SCM007
NDA 20-710/SCM011

INFORMATION REQUEST LETTER

SmithKline Beecham Pharmaceuticals
Attention: Deborah E. Zuber, R.Ph.
Assistant Director, NA Regulatory Affairs
1250 South Collegeville Road, P.O. Box 4089
Collegeville, PA 19426-0989

Dear Ms. Zuber:

Please refer to your supplemental new drug applications submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Paxil® Tablets, Paxil® Capsules, Paxil® CR Tablets, Paxil® Oral Suspension. We also refer to your submissions dated February 15, 2001.

We are reviewing the Chemistry section of your submissions and have the following comments and information requests. We need your prompt written response to continue our evaluation of your supplemental application.

1. (b) (4)

A deficiency letter has been sent to SKB for DMF's 14475 and 15039. The review of these supplements is pending response and evaluation to the question stated above and the DMF deficiency letter.

If you have any questions, call Paul David, R.Ph., Regulatory Project Manager, at (301) 594-5530.

Sincerely,

{See appended electronic signature page}

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

/s/

Robert H. Seevers
3/23/01 08:56:21 AM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-936/S007

20-031/S034

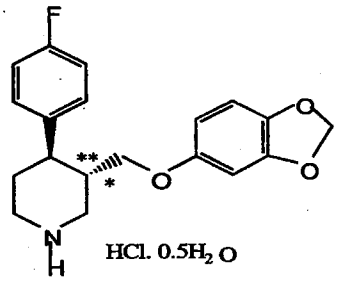
20-710/S011

20-885/S004

CHEMISTRY REVIEW(S)

CHEMIST REVIEW
OF **SUPPLEMENTS**

1. ORGANIZATION:	HFD-120
2. NDA:	**20-031, 20-885 20-936, 20-710**
3. SUPPLEMENT NUMBERS/ DATES:	**SCM034, SCM004, SCM007, SCM011 respectively**
letter date:	December 29, 2000
stamp date:	January 3, 2001
4. AMENDMENTS/REPORTS/DATES:	
5. RECEIVED BY CHEMIST:	January 7, 2001
6. APPLICANT NAME & ADDRESS	Smithkline Beecham Pharmaceuticals 1250 S. Collegeville Road, PO Box 5089, PA 19426-0989
7. NAME OF DRUG:	Paxil®
8. NONPROPRIETARY NAME:	Paroxetine hydrochloride
9. CHEMICAL NAME/STRUCTURE:	(-)trans-4R-(4'-fluorophenyl)-3S-[3',4'-methylenedioxyphenoxymethyl]-piperidine hydrochloride hemihydrate



10. DOSAGE FORM(S):	N20-031 – Paxil® Tablets N20-885 – Paxil® Capsules N20-936 – Paxil® CR Tablets N20-710 – Paxil® Oral Suspension
11. POTENCY:	N20-031 – Paxil® Tablets (10, 20, 30, 40 mg) N20-885 – Paxil® Capsules (10, 20, 30, 40 mg) N20-936 – Paxil® CR Tablets (12.5 and 25 mg) N20-710 – Paxil® Oral Suspension (10 mg/5 mL)
12. PHARMACOLOGICAL CATEGORY:	Depression, Obsessive Compulsive Disorder, and Panic Disorder
13. HOW DISPENSED:	X (Rx) _____ (OTC)
14. RECORDS & REPORTS CURRENT:	X Yes _____ No
15. RELATED IND/NDA/DMF:	DMF 15039 and 14475

SUPPLEMENT PROVIDES FOR:
Prior Approval supplements for use of an alternate modified route of manufacture (b) (4) of paroxetine HCl using (b) (4) The changes in manufacture will affect two DMF's for paroxetine HCl (b) (4) DMF # 14475 and DMF # 15039.

COMMENTS:
These PA supplements were initially accidentally filed as an amendment to another Paxil supplement. This was corrected on March 1, 2001. An IR letter was sent to SKB (GSK) on February 8, 2001 for information

regarding these PA supplements. However, the IR letter and response refer to the earlier supplements N20-031/SCM032, N20-885/SCM003, N20-936/SCM006 and N20-710/SCM010. The response to IR sent on February 15, 2001 for N20-031/SCM032, N20-885/SCM003, N20-936/SCM006 and N20-710/SCM010 is evaluated in this review.

CONCLUSIONS & RECOMMENDATIONS:
N20-031/SCM034, N20-710/SCM011, N20-885/SCM004, N20-936/SCM007 are recommended **APPROVABLE** contingent on the response and evaluation of the deficiencies. Please see attached review notes and deficiency letter for DMF's 14475 and 15039 dated March 19, 2001 for details.

19. REVIEWER NAME	SIGNATURE	DATE COMPLETED
Gurpreet Gill-Sangha, Ph.D. Review Chemist, HFD-120	_____	_____
Robert H. Seevers, Ph.D. Chemistry Team Leader, HFD-120	_____	_____

Cc:
NDA 20-031/SCM034
NDA 20-885/SCM004
NDA 20-936/SCM007
NDA 20-710/SCM011
HFD-120/Division File
HFD-120/GGill-Sangha
HFD-120/PDavid
HFD-120/RSeevers
File: C:/data/My Documents/data gill/supplement NDA/20-031-710-936-885/rev1-34-11-7-4.doc

6 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Chemistry- 20-936 S007

/s/

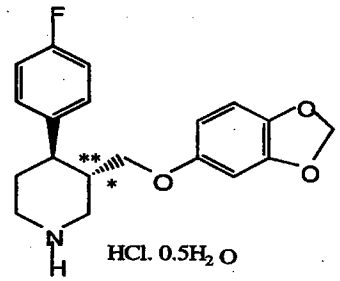
Gurpreet Gill-Sangha
3/22/01 12:50:01 PM
CHEMIST

This is review #1 for all 4 PA supplements with the response to IR letter

Robert H. Seevers
3/22/01 01:00:48 PM
CHEMIST

CHEMIST REVIEW
OF **SUPPLEMENTS**

1. ORGANIZATION:	HFD-120
2. NDA:	**20-031, 20-885 20-936, 20-710**
3. SUPPLEMENT NUMBERS/ DATES:	**SCM034, SCM004, SCM007, SCM011 respectively**
letter date:	December 29, 2000
stamp date:	January 3, 2001
4. AMENDMENTS/REPORTS/DATES:	April 23, 2001
5. RECEIVED BY CHEMIST:	January 7, 2001/April 20, 2001 by Fax
6. APPLICANT NAME & ADDRESS	Smithkline Beecham Pharmaceuticals 1250 S. Collegeville Road, PO Box 5089, PA 19426-0989
7. NAME OF DRUG:	Paxil®
8. NONPROPRIETARY NAME:	Paroxetine hydrochloride
9. CHEMICAL NAME/STRUCTURE:	(-)trans-4R-(4'-fluorophenyl)-3S-[3',4'-methylenedioxyphenoxymethyl]-piperidine hydrochloride hemihydrate



10. DOSAGE FORM(S):	N20-031 – Paxil® Tablets N20-885 – Paxil® Capsules N20-936 – Paxil® CR Tablets N20-710 – Paxil® Oral Suspension
11. POTENCY:	N20-031 – Paxil® Tablets (10, 20, 30, 40 mg) N20-885 – Paxil® Capsules (10, 20, 30, 40 mg) N20-936 – Paxil® CR Tablets (12.5 and 25 mg) N20-710 – Paxil® Oral Suspension (10 mg/5 mL)
12. PHARMACOLOGICAL CATEGORY:	Depression, Obsessive Compulsive Disorder, and Panic Disorder
13. HOW DISPENSED:	X (R_X) _____ (OTC)
14. RECORDS & REPORTS CURRENT:	X Yes _____ No
15. RELATED IND/NDA/DMF:	DMF 15039 and 14475

SUPPLEMENT PROVIDES FOR:

Prior Approval supplements for use of an alternate modified route of manufacture (b) (4) of paxoretine HCl using (b) (4) method. The changes in manufacture will affect DMF's 14475 and 15039 for paroxetine HCl (b) (4)

COMMENTS:
Responses to the deficiency letter for DMF's 15039 and 14475 are evaluated in the respective DMF CR#2 that are attached to this review. Response to the IR letter for these PA supplements dated 3/22/01 is evaluated in this review.

CONCLUSIONS & RECOMMENDATIONS:
N20-031/SCM034, N20-710/SCM011, N20-885/SCM004, N20-936/SCM007 are to be recommended **APPROVED** with the noted comments and commitments.

19. REVIEWER NAME	SIGNATURE	DATE COMPLETED
Gurpreet Gill-Sangha, Ph.D. Review Chemist, HFD-120	_____	_____
Robert H. Seevers, Ph.D. Chemistry Team Leader, HFD-120	_____	_____

Cc:
NDA 20-031/SCM034
NDA 20-885/SCM004
NDA 20-936/SCM007
NDA 20-710/SCM011
HFD-120/Division File
HFD-120/GGill-Sangha
HFD-120/PDavid
HFD-120/RSeevers
File: C:/data/My Documents/data gill/supplement NDA/20-031-710-936-885/rev2-34-11-7-4.doc

25 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Chemistry- 20-936 S007

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Gurpreet Gill-Sangha
4/30/01 10:50:19 AM
CHEMIST

4 PA supplements review #2

Robert H. Seevers
4/30/01 12:08:38 PM
CHEMIST

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-936/S007

20-031/S034

20-710/S011

20-885/S004

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-031/S-034
NDA 20-710/S-011
NDA 20-885/S-004
NDA 20-936/S-007

PRIOR APPROVAL SUPPLEMENT

SmithKline Beecham Pharmaceuticals
Attention: Deborah Zuber, R.Ph.
Assistant Director, Regulatory Affairs, N.A.
1250 Collegeville Road
PO Box 5089
Collegeville, PA 19426-0989

Dear Ms. Zuber:

We have received your supplemental drug applications submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

NDA Number	Supplement Number	Drug Name
20-031	S-034	Paxil (paroxetine hydrochloride hemihydrate) Tablets 10 mg, 20 mg, 30 mg, and 40 mg
20-710	S-011	Paxil (paroxetine hydrochloride hemihydrate) Oral Suspension
20-885	S-004	Paxil (paroxetine hydrochloride hemihydrate) Capsules 10 mg, 20 mg, 30 mg, and 40 mg
20-936	S-007	Paxil (paroxetine hydrochloride hemihydrate) CR Tablets 12.5 mg and 25 mg

Date of Supplements: December 29, 2000

Date of Receipt: January 3, 2001

These supplements propose the following change: a modification of the method of drug substance manufacture.

Unless we notify you within 60 days of our receipt date that the applications are not sufficiently complete to permit a substantive review, these applications will be filed under section 505(b) of the Act on March 4, 2001 in accordance with 21 CFR 314.101(a). If the applications are filed, the primary user fee goal date will be May 3, 2001 and the secondary user fee goal date will be July 3, 2001.

Please cite the application numbers listed above at the top of the first page of any communications concerning these applications. All communications concerning these supplemental applications should be addressed as follows:

U.S. Postal Service:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Neuropharmacological Drug Products, HFD-120
Attention: Division Document Room 4008
5600 Fishers Lane
Rockville, Maryland 20857

Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Neuropharmacological Drug Products, HFD-120
Attention: Division Document Room 4008
1451 Rockville Pike
Rockville, Maryland 20852-1420

If you have any questions, call Paul David, R.Ph., Regulatory Project Manager, at (301) 594-5530.

Sincerely,

{See appended electronic signature page}

Robert H. Seevers, Ph.D.
Chemistry Team Leader, Psychiatric Drugs for the Division of Neuropharmacological Drug Products, HFD-120
DNDC 1, Office of New Drug Chemistry
Center for Drug Evaluation and Research

/s/

Robert H. Seevers
2/28/01 03:55:12 PM