CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-515

CHEMISTRY REVIEW(S)

NDA 21-515

Wellbutrin (bupropion hydrochloride)
Extended Release Tablets

GlaxoSmithKline, Inc

Sherita D. McLamore, Ph.D.
Division of Neuropharmacological Drug Products
HFD-120

Table of Contents

Chemistry Review Data Sheet

1. NDA 21-515

2. REVIEW # 4

3. REVIEW DATE: 8/29/03

4. REVIEWER: Sherita McLamore, Ph.D.

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Original Submission	8/26/02
Amendment	2/11/03
Amendment	4/17/03
CMC Review #1	6/10/03
CMC Review #2	6/10/03
CMC Review #3	8/16/03

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Response to Approvable letter	7/03/03

7. NAME & ADDRESS OF APPLICANT:

Name:	GlaxoSmithKline
Address:	One Franklin Plaza P.O. Box 7929 Philadelphia, PA 19101
Representative:	Mary E. Martinson
Telephone:	919.315.8319

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: Wellbutrin XL™
b) Non-Proprietary Name / USAN: bupropion hydrochloride
c) Code Name/# (ONDC only): N/A
d) Chem. Type/Submission Priority (ONDC only):

- Chem. Type: 3
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505(b)(1)

10. PHARMACOL. CATEGORY: Treatment of major depressive disorder

11. DOSAGE FORM: Extended Release Tablets

12. STRENGTH/POTENCY: 150 mg and 300 mg

13. ROUTE OF ADMINISTRATION: oral

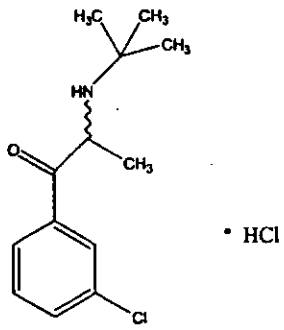
14. Rx/OTC DISPENSED: __X__Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
_____SPOTS product – Form Completed

__X___Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name: (±)-2-(tert-butylamino)-3'-chloropropiophenone hydrochloride
Molecular Formula: $C_{13}H_{18}ClNO \bullet HCl$
Molecular Weight: 276.20



• HCl

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
	Type II			1	Adequate	03-25-03	N/A
	Type III			1	Adequate	9-26-00	N/A
	Type III			1	Adequate	9-28-00	N/A
	Type III			1	Adequate	8-7-97	N/A
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	Type III			1	Adequate	3-20-01	N/A
	Type III			1	Adequate	06-11-99	N/A

[1] Action codes for DMF:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 –Type 1 DMF

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6 – DMF not available

7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
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IND	13,845	Wellbutrin® (bupropion hydrochloride) Tablets-antidepressant
IND	36,571	Bupropion Hydrochloride -cocaine dependence
IND	45,794	Bupropion Hydrochloride-smoking cessation
NDA	18-644	Wellbutrin® Tablets
NDA	20-358	Wellbutrin SR® Tablets

18. STATUS:

ONDC:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	N/A	N/A	N/A
EES	Acceptable	4/21/03	Office of Compliance
Pharm/Tox	N/A	N/A	N/A
Biopharm	Acceptable pending outcome of DSI inspection	5/12/03	Sally Yasuda
Methods Validation	Pending	Pending	Sherita McLamore, Ph.D.
DMETS	Acceptable	5/9/03	Jennifer Fan, Pharm.D.
EA	Categorical Exclusion Granted	5/25/05	Sherita McLamore, Ph.D
Microbiology	N/A	N/A	N/A

The Chemistry Review for NDA 21-515

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The Chemistry, Manufacturing, and Controls (CMC) section of NDA 21-515 is complete has been approved.

Methods validation will be submitted.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Bupropion Hydrochloride was originally investigated under IND 13,845. Bupropion is a racemate and is a member of the aminoketone class of compounds. Bupropion Hydrochloride is currently approved for use in Welbutrin SR® Tablets (NDA 20-358) and Wellbutrin Tablets (NDA 18-644). The applicant included very limited information on the drug substance in this application and references [redacted] for the manufacture and controls of

the drug substance. The drug substance is described as a white crystalline solid that is highly soluble in water and has a bitter taste. Bupropion hydrochloride is designated as (±)-1-(3-chlorophenyl)-2-[(1,1-dimethylethy) amino]-1-propanone hydrochloride. The molecular formula for is $C_{13}H_{18}ClNO\cdot HCl$ and the molecular weight is 276.2. A letter of authorization is provided on page 2 of volume 4.1. There is no information pertaining to the synthesis of the drug substance outlined in this application. The applicant intends to adopt the current USP (effective January 1, 2003) specifications for the drug substance

The drug product, Wellbutrin XL™ Tablets, is an antidepressant designed for once a day administration. The drug product, Wellbutrin XL™, is a [redacted] tablet consisting of [redacted] Together, the coatings form a [redacted] that is responsible for the release of the drug substance, bupropion hydrochloride. All ingredients used in the manufacture of the drug product with the exception of [redacted] Black Ink are either USP or NF grade. The applicant indicates that the drug product will be available in two dosages 150 mg and 300 mg and will be manufactured at the Biovail Lifesciences in Steinbach, CA. The 150 mg tablets are creamy white to pale yellow round tablet imprinted with "Wellbutrin XL 150" in black ink on one side and plain on the other side. The 300 mg tablets are creamy white to pale yellow round tablet imprinted with "Wellbutrin XL 300" in black ink on one side and plain on the other side. The tablets will be packaged in 7 count [redacted] bottles for physician samples and 30 count [redacted] bottles for commercial distribution. Both the 30 and 7 count bottles will be packaged with a combination [redacted] and closed with a [redacted] child resistant closure.

The applicant proposed the proprietary name Wellbutrin XL™ Tablets for the drug product. The Office of Post–Marketing Drug Risk Assessment (OPDRA) has not posed any objections to the use of this name.

B. Description of How the Drug Product is Intended to be Used

Wellbutrin XL™ is being developed for the treatment major depressive disorder. It's extended release formulation is designed for patients that suffer from MDD. The applicant has provided a confirmatory bioequivalence study comparing Wellbutrin XL™ Tablets with the currently marketed Wellbutrin® Tablets. The applicant indicates that administration should begin with the 150 mg dose and if that dose is well tolerated then the patient should increase to the 300 mg/day target dose. The applicant further indicates that an increase to the maximum daily dose of 450 mg/day may be given as a single dose or divided doses.

The applicant has requested a [redacted] expiry for the 150 and 300 mg tablets in the 7 and 30 bottles. The applicant provided 6 months of accelerated (40°C/75% RH) stability data together with 12 months of long term (30°C/60% RH) and intermediate (30°C/60% RH) stability data on six [redacted] batches of the drug product in each of the proposed commercial packages. The applicant updated the dissolution specification from the original submission.

The original dissolution specifications were 2 hours: [redacted]; 4 hours: [redacted]; 8 hours: [redacted] and 16 hours [redacted] The new dissolution specifications are 2 hours: [redacted] 4 hours: [redacted] 8 hours: [redacted] and 16 hours [redacted]. Based on the new dissolution specification, there were [redacted] at the 8 hour time point at 30°C/60% RH and 40°C/75% RH (see stability section of this review). Based on the information provided in this application, the applicant has not provide enough data to support a [redacted] expiry. The applicant will be granted an **12 month expiry** for the 150 and 300 mg tablets in the 7 and 30 bottles.

C. Basis for Approvability or Not-Approval Recommendation

NDA 21-515 is recommended for approval from a CMC standpoint.

III. Administrative

A. Reviewer's Signature

B. Endorsement Block

SMcLamore/Date
TOliver (TL)/Date
A (PM)/Date

C. CC Block

Orig. NDA 21-515
HFD-120/Division File
HFD-120/DBates
HFD-120/SMcLamore
HFD-120/TOliver

APPEARS THIS WAY ON ORIGINAL

2 Page(s) Withheld

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

_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

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

/s/

Sherita McLamore
8/29/03 01:18:50 PM
CHEMIST

Thomas Oliver
8/29/03 01:56:22 PM
CHEMIST

APPEARS THIS WAY
ON ORIGINAL

ESTABLISHMENT EVALUATION REQUEST

DETAIL REPORT

Application:	NDA 21515/000	Action Goal:	
Stamp:	26-AUG-2002	District Goal:	27-APR-2003
Regulatory Due:	03-SEP-2003	Brand Name:	WELLBUTRIN XL(BUPROPION
Applicant:	SMITHKLINE BEECHAM CORP DBA GL	Estab. Name:	HCL)EXTENDED REL
	1 FRANKLIN PLAZA	Generic Name:	BUPROPION HCL EXTENDED
	PHILADELPHIA, PA 19101		RELEASE TABLETS
Priority:	3S	Dosage Form:	(TABLET)
Org Code:	120	Strength:	150 MG AND 300 MG

Application Comment:

FDA Contacts:	D. BATES	(HFD-120)	301-594-5536	, Project Manager
	S. MCLAMORE	(HFD-810)	301-594-5359	, Review Chemist
	T. OLIVER	(HFD-810)	301-594-2570	, Team Leader

Overall Recommendation: ACCEPTABLE on 31-JUL-2003by S. FERGUSON(HFD-322)301-827-9009

ACCEPTABLE on 21-APR-2003by S. FERGUSON(HFD-322)301-827-9009

Establishment: CFN 9615235 FEI 3002806613

BIOVAIL LIFESCIENCES

STEINBACH, MANITOBA, CA

DMF No: AADA:

Responsibilities: FINISHED DOSAGE MANUFACTURER

FINISHED DOSAGE PACKAGER

FINISHED DOSAGE RELEASE TESTER

FINISHED DOSAGE STABILITY TESTER

Profile: TCT OAI Status: NONE

EM	stone Name	Date	Type	Insp. Date	Decision & Reason	Creator
	SUBMITTED TO OC	27-SEP-2002				MCLAMORES
	SUBMITTED TO DO	30-SEP-2002	GMP			DAMBROGIOJ
	DO RECOMMENDATION	07-OCT-2002			ACCEPTABLE	DAMBROGIOJ

BASED ON FILE REVIEW

OC RECOMMENDATION 08-OCT-2002 ACCEPTABLE DAMBROGIOJ

DISTRICT RECOMMENDATION

Establishment: [redacted]

DMF No: AADA:

Responsibilities: [redacted]

Profile: CSN OAI Status: NONE

Estab. Comment:

APPEARS THIS WAY
ON ORIGINAL

ESTABLISHMENT EVALUATION REQUEST

DETAIL REPORT

Milestone Name	Date	Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	27-SEP-2002				MCLAMORES
OC RECOMMENDATION	30-SEP-2002			ACCEPTABLE BASED ON PROFILE	DAMBROGIOJ

Establishment: CFN 1033964 FEI 1033964
GLAXO INC
1011 NORTH ARENDELL AVE
ZEBULON, NC 27597

DMF No: AADA:

Responsibilities: FINISHED DOSAGE PACKAGER

Profile: TCT OAI Status: NONE

Milestone Name	Date	Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	27-SEP-2002				MCLAMORES
SUBMITTED TO DO	27-SEP-2002	GMP			FERGUSONS
ASSIGNED INSPECTION T	12-NOV-2002	PS			LANDREWS
INSPECTION SCHEDULED	14-NOV-2002		26-APR-2003		LANDREW1@OR
INSPECTION PERFORMED	17-APR-2003		17-APR-2003		LANDREWS
INSPECTION PERFORMED	17-APR-2003		17-APR-2003		LANDREW1@OR
AUTOMATIC WITHHOLD STATUS ISSUED BY FACTS, DUE TO FIRM BEING OUT OF BUSINESS OR MERGED					
DO RECOMMENDATION	21-APR-2003			ACCEPTABLE INSPECTION	LANDREWS
INSPECTION CONDUCTED ON 4/15-17/03. NO 483 ISSUED. PROFILE CLASS IS ACCEPTABLE.					
OC RECOMMENDATION	21-APR-2003			ACCEPTABLE DISTRICT RECOMMENDATION	FERGUSONS
DO RECOMMENDATION	31-JUL-2003			ACCEPTABLE DUPLICATE MILESTONE FROM FACTS	LANDREWS
OC RECOMMENDATION	31-JUL-2003			ACCEPTABLE	FERGUSONS

Establishment: CFN [redacted] FEI

[redacted]

[redacted]

DMF No: AADA:

Responsibilities:

Profile: CTL OAI Status: NONE

EMilestone Name	Date	Type	Insp. Date	Decision & Reason	Creator

ESTABLISHMENT EVALUATION REQUEST

DETAIL REPORT

SUBMITTED TO OC	27-SEP-2002		MCLAMORES
OC RECOMMENDATION	30-SEP-2002	ACCEPTABLE	DAMBROGIOJ
		BASED ON PROFILE	

APPEARS THIS WAY
ON ORIGINAL

NDA 21-515

Wellbutrin (bupropion hydrochloride)
Extended Release Tablets

GlaxoSmithKline, Inc

Sherita D. McLamore, Ph.D.
Division of Neuropharmacological Drug Products
HFD-120

Table of Contents

Chemistry Review Data Sheet

1. NDA 21-515

2. REVIEW # 3

3. REVIEW DATE: 8/15/03

4. REVIEWER: Sherita McLamore, Ph.D.

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Original Submission	8/26/02
Amendment	2/11/03
Amendment	4/17/03
CMC Review #1	6/10/03
CMC Review #2	6/10/03

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Response to Approvable letter	7/03/03

7. NAME & ADDRESS OF APPLICANT:

Name: GlaxoSmithKline

Address: One Franklin Plaza
P.O. Box 7929
Philadelphia, PA 19101

Representative: Mary E. Martinson

Telephone: 919.315.8319

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: Wellbutrin XL™
b) Non-Proprietary Name / USAN: bupropion hydrochloride
c) Code Name/# (ONDC only): N/A
d) Chem. Type/Submission Priority (ONDC only):

- Chem. Type: 3
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505(b)(1)

10. PHARMACOL. CATEGORY: Treatment of major depressive disorder

11. DOSAGE FORM: Extended Release Tablets

12. STRENGTH/POTENCY: 150 mg and 300 mg

13. ROUTE OF ADMINISTRATION: oral

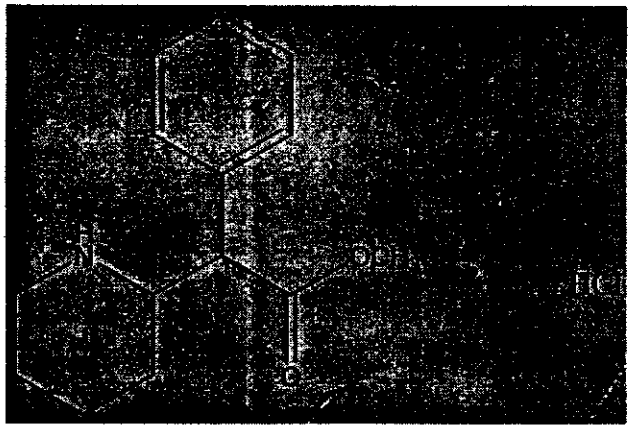
14. Rx/OTC DISPENSED: __X__Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
_____SPOTS product – Form Completed

__X___Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name: (±)-2-(tert-butylamino)-3'-chloropropiophenone hydrochloride
Molecular Formula: $C_{13}H_{18}ClNO \bullet HCl$
Molecular Weight: 276.20



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
	Type II			1	Adequate	03-25-03	N/A
	Type III			1	Adequate	9-26-00	N/A
	Type III			1	Adequate	9-28-00	N/A
	Type III			1	Adequate	8-7-97	N/A
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[1] Action codes for DMF Table:
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B. Other Documents:

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NDA	20-358	Wellbutrin SR® Tablets

18. STATUS:

ONDC:

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Biometrics	N/A	N/A	N/A
EES	Acceptable	4/21/03	Office of Compliance
Pharm/Tox	N/A	N/A	N/A
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The Chemistry Review for NDA 21-515

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C. Basis for Approvability or Not-Approval Recommendation

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III. Administrative

A. Reviewer's Signature

B. Endorsement Block

SMcLamore/Date
TOliver (TL)/Date
A (PM)/Date

C. CC Block

Orig. NDA 21-515
HFD-120/Division File
HFD-120/DBates
HFD-120/SMcLamore
HFD-120/TOliver

7 Page(s) Withheld

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

_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

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

/s/

Sherita McLamore
8/15/03 02:40:06 PM
CHEMIST

Thomas Oliver
8/15/03 02:49:07 PM
CHEMIST

APPEARS THIS WAY
ON ORIGINAL

NDA 21-515

Wellbutrin (bupropion hydrochloride)
Extended Release Tablets

GlaxoSmithKline, Inc

Sherita D. McLamore, Ph.D.
Division of Neuropharmacological Drug Products
HFD-120

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1. NDA 21-515

2. REVIEW # 1

3. REVIEW DATE: 5/23/03

4. REVIEWER: Sherita McLamore, Ph.D.

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
None	

6. SUBMISSION(S) BEING REVIEWED:

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Amendment	2/11/03
Amendment	4/17/03

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Representative:	Mary E. Martinson
Telephone:	919.315.8319

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c) Code Name/# (ONDC only): N/A
d) Chem. Type/Submission Priority (ONDC only):

- Chem. Type: 3
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505(b)(1)

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11. DOSAGE FORM: Extended Release Tablets

12. STRENGTH/POTENCY: 150 mg and 300 mg

13. ROUTE OF ADMINISTRATION: oral

14. Rx/OTC DISPENSED: __X__Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM)[Note24]:

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16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

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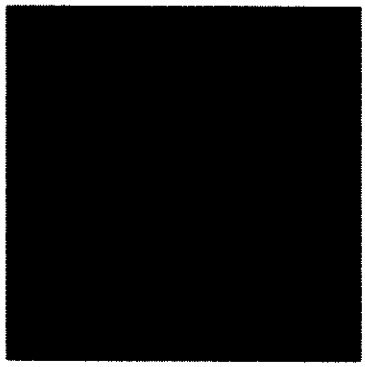
Molecular Weight: 276.20



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
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	Type III			1	Adequate	9-26-00	N/A
[redacted]	Type III	[redacted]	[redacted]	1	Adequate	9-28-00	N/A
	Type III			1	Adequate	8-7-97	N/A
[redacted]	Type III		[redacted]	1	Adequate	3-2-00	N/A
	Type III	[redacted]		1	Adequate	3-20-01	N/A
[redacted]	Type III	[redacted]	[redacted] ( )	1	Adequate	06-11-99	N/A

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
IND	28,676	Wellbutrin SR® (bupropion hydrochloride) Sustained Releases Tablets-antidepressant
IND	13,845	Wellbutrin ® (bupropion hydrochloride) Tablets-antidepressant
IND	36,571	Bupropion Hydrochloride -cocaine dependence
IND	45,794	Bupropion Hydrochloride-smoking cessation
NDA	18-644	Wellbutrin® Tablets
NDA	20-358	Wellbutrin SR® Tablets

18. STATUS:

ONDC:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	N/A	N/A	N/A
EES	Acceptable	4/21/03	Office of Compliance
Pharm/Tox	N/A	N/A	N/A
Biopharm	Acceptable pending outcome of DSI inspection	5/12/03	Sally Yasuda
Methods Validation	Pending	Pending	Sherita McLamore, Ph.D.
DMETS	Acceptable	5/9/03	Jennifer Fan, Pharm.D.
EA	Categorical Exclusion Granted	5/25/05	Sherita McLamore, Ph.D
Microbiology	N/A	N/A	N/A

The Chemistry Review for NDA 21-515

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The Chemistry, Manufacturing, and Controls (CMC) section of NDA 21-515 is approvable. The applicant will been sent a list of deficiencies and comments.

Methods validation will be submitted after all CMC deficiencies have been addressed.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Bupropion Hydrochloride was originally investigated under IND 13,845. Bupropion is a racemate and is a member of the aminoketone class of compounds. Bupropion Hydrochloride is currently approved for use in Welbutrin SR® Tablets (NDA 20-358) and Wellbutrin Tablets (NDA 18-644). The applicant included very limited information on the drug substance in this application and references [redacted] for the manufacture and controls of the drug substance. The drug substance is described as a white crystalline solid that is highly soluble in water and has a bitter taste. Bupropion hydrochloride is designated as (±)-1-(3-chlorophenyl)-2-[(1,1-dimethylethy) amino]-1-propanone hydrochloride. The molecular formula for is $C_{13}H_{18}ClNO\cdot HCl$ and the molecular weight is 276.2. A letter of authorization is provided on page 2 of volume 4.1. There is no information pertaining to the synthesis of the drug substance outlined in this application. The applicant intends to adopt the current USP (effective January 1, 2003) specifications for the drug substance

The drug product, Wellbutrin XL™ Tablets, is an antidepressant designed for once a day administration. The drug product, Wellbutrin XL™, is a [redacted] tablet consisting of [redacted] Together, the coatings form a [redacted] that is responsible for the release of the drug substance, bupropion hydrochloride. All ingredients used in the manufacture of the drug product with the exception of [redacted] Black Ink are either USP or NF grade. The applicant indicates that the drug product will be available in two dosages 150 mg and 300 mg and will be manufactured at the Biovail Lifesciences in Steinbach, CA. The 150 mg tablets are creamy white to pale yellow round tablet imprinted with "Wellbutrin XL 150" in black ink on one side and plain on the other side. The 300 mg tablets are creamy white to pale yellow round tablet imprinted with "Wellbutrin XL 300" in black ink on one side and plain on the other side. The tablets will be packaged in 7 count [redacted] bottles for physician samples and 30 count [redacted] bottles for commercial distribution. Both the 30 and 7 count bottles will be packaged with a [redacted] and closed with a [redacted] child resistant closure.

The applicant proposed the proprietary name Wellbutrin XL™ Tablets for the drug product. The Office of Post–Marketing Drug Risk Assessment (OPDRA) has not posed any objections to the use of this name.

B. Description of How the Drug Product is Intended to be Used

Wellbutrin XL™ is being developed for the treatment major depressive disorder. It's extended release formulation is designed for patients that suffer from MDD. The applicant has provided a confirmatory bioequivalence study comparing Wellbutrin XL™ Tablets with the currently marketed Wellbutrin® Tablets. The applicant indicates that administration should begin with the 150 mg dose and if that dose is well tolerated then the patient should increase tot he 300 mg/day target dose. The applicant further indicates that an increase to the maximum daily dose of 450 mg/day may be given as a single dose or divided doses.

The applicant has requested a [redacted] expiry for the 150 and 300 mg tablets in the 7 and 30 bottles. The applicant has provided 6 months of accelerated stability data together with 12 months of long term and intermediate stability data on six [redacted] batches of the drug product in each of the proposed commercial packages. All stability data was within the applicants propose specifications.

C. Basis for Approvability or Not-Approval Recommendation

NDA 21-515 is Approvable from a Chemistry standpoint due to chemistry, manufacturing and controls concerns related to the drug substance and the drug product as outlined in this review.

III. Administrative

A. Reviewer's Signature

B. Endorsement Block

SMcLamore/Date
TOliver (TL)/Date
A (PM)/Date

C. CC Block

Orig. NDA 21-515
HFD-120/Division File
HFD-120/DBates
HFD-120/SMcLamore
HFD-120/TOliver