

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

NDA 21-436/S-004

Trade Name: Abilify Tablets

Generic Name: Aripiprazole

Sponsor: Otsuka America Pharmaceutical, Inc. and
Bristol-Myers Squibb Company

Approval Date: 12/30/03

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APPLICATION NUMBER:
NDA 21-436/S-004

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Reviews / Information Included in this NDA Review.

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Microbiology Review(s)	
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APPLICATION NUMBER:
NDA 21-436/S-004

APPROVAL LETTER



NDA 21-436/S-004

Otsuka Pharmaceuticals Co. Ltd.
Dr. Kusuma Mallikaarjun
Director, Regulatory Affairs
2440 Research Blvd
Rockville, MD 20850

Dear Dr. Mallikaarjun:

Please refer to your supplemental new drug application dated July 2, 2003, received July 3, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Abilify™ (aripiprazole) Tablets, 2, 5, 10, 15, 20 and 30 mg.

This "Changes Being Effected in 30 days" supplemental new drug application provides for the addition of Bristol-Myers Squibb of Mayaguez, Puerto Rico (CFN 2627673) as an alternate site of manufacture for Abilify® Tablets.

We have completed the review of this supplemental 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, call Steve Hardeman, Regulatory Project Manager, at (301) 594-5536.

Sincerely,

{See appended electronic signature page}

Thomas Oliver, 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

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/s/

Thomas Oliver
12/30/03 12:46:44 PM

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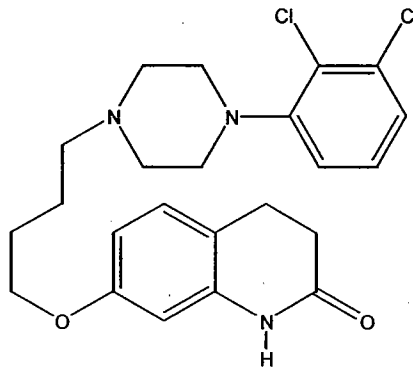
APPLICATION NUMBER:
NDA 21-436/S-004

CHEMISTRY REVIEW(S)

CHEMIST REVIEW
OF SUPPLEMENT

1. ORGANIZATION: HFD-120
2. NDA 21-436
3. SUPPLEMENT NUMBER AND DATES: SCM-004
LETTER DATE: 07-02-03
STAMP DATE: 07-03-03
4. AMENDMENT/REPORTS/DATES
5. RECEIVED BY CHEMIST: 07-15-03

6. APPLICANT NAME & ADDRESS: Otsuka America Pharmaceutical, Inc.
2440 Research Blvd.
Rockville, MD 20850
7. NAME OF DRUG: Abilify® Tablets
8. NONPROPRIETARY NAME: Aripiprazole
9. CHEMICAL NAME and STRUCTURE: 7-[4-[4-(2,3-Dichlorophenyl)-1-piperazinyl]butoxy]-3,4-dihydrocarbostyryl



10. DOSAGE FORMS: Tablets
11. POTENCY: 2 mg, 5 mg, 10 mg,, 15 mg, 20 mg and 30 mg
12. PHARMACOLOGICAL CATEGORY: Schizophrenia
13. HOW DISPENSED: (Rx) (OTC)
14. RECORD and REPORTS CURRENT: Yes No
15. RELATED IND/NDA/DMF: none

16. SUPPLEMENT PROVIDES FOR: This supplement provides for Bristol-Myers Squibb (BMS) of Mayaguez, Puerto Rico (CFN 2627673) as an alternate site of manufacture for Abilify® Tablets. The applicant indicates that this site will also perform packaging and release testing. This site change qualifies as a level 3 change according to the SUPAC-IR guidance to industry.

17. ADDITIONAL COMMENTS: The applicant seeks to add Bristol-Myers Squibb (BMS) of Mayaguez, Puerto as an alternate supplier and packager 2 mg, 5 mg, 10 mg,, 15 mg, 20 mg and 30 mg drug product. The applicant indicates that the site currently has a satisfactory cGMP in accordance with title 21 of the CFR 210 and 211. The inspection request was submitted to EER on July 15, 2003 and was found acceptable based on profile on July 25, 2003. The applicant included up to 18 months of stability data for the 2, 5, 10 and 15 mg tablets manufactured at the new facility packaged in 30 count bottles and blisters and 3 months of stability data for 20 and 30 mg tablets packaged in 30 count bottles and blisters. The applicant also includes a comparative dissolution analysis, batch records and a certificate of analysis for each dosage strength of the drug product. The applicant further indicates that there were no changes in the drug substance or in the drug product composition or method of manufacture. In addition to the site change, the applicant proposes the use of an alternate closure and includes the appropriate data (i.e. DMF reference and LOA) to support this change.

18. CONCLUSIONS & RECOMMENDATIONS:

Based on the OC Recommendation and from a CMC perspective, it is recommended that this supplement be **APPROVED**.

Sherita D. McLamore, Ph.D.
Review Chemist

Signature

Date Completed

Robert Seevers, Ph.D.
Chemistry Team Leader

Signature

Date

Redacted 7 page(s)

of trade secret and/or

confidential commercial

information from

Soot Chemistry Review

29-DEC-2003

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

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Application : NDA 21436/004
Org Code : 120
Priority : IS

Sponsor: OTSUKA PHARM
2440 RESEARCH BLVD
ROCKVILLE, MD 20850

Stamp Date : 03-JUL-2003
PDUFA Date : 03-JAN-2004
Action Goal :
District Goal: 29-NOV-2003

Brand Name : ABILIFY (ARIPRAZOLE)
10/15/20/30MG
Estab. Name:
Generic Name: ARIPIPRAZOLE
Dosage Form: (TABLET)
Strength : 2, 5, 10, 15, 20, 30 MG

FDA Contacts: S. HARDEMAN
S. MCLAMORE
T. OLIVER

Project Manager (HFD-120) 301-594-5525
Review Chemist (HFD-810) 301-594-5359
Team Leader (HFD-810) 301-594-5551

Overall Recommendation: ACCEPTABLE on 25-JUL-2003 by S. FERGUSON (HFD-322) 301-827-9009

Establishment : CFN : 2627673 FEI : 2627673
BRISTOL LABORATORIES INC DIV BRISTOL MYERS CO
FOREIGN TRADE ZONE 7 RD 114
MAYAGUEZ, PR 00680

DMF No: AADA:

Responsibilities: FINISHED DOSAGE MANUFACTURER
FINISHED DOSAGE PACKAGER
FINISHED DOSAGE RELEASE TESTER

Profile : TCM OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 25-JUL-03
Decision : ACCEPTABLE
Reason : DISTRICT RECOMMENDATION

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/s/

Sherita McLamore
1/14/04 12:40:07 PM
CHEMIST

Thomas Oliver
1/14/04 12:44:42 PM
CHEMIST

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APPLICATION NUMBER:
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ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-436/S-004

CBE-30 SUPPLEMENT

Otsuka America Pharmaceutical Inc.
Attn: Dr. Kusuma Mallikaarjun
Director, Regulatory Affairs/Abilify™
2440 Research Boulevard
Rockville, MD 20850

Dear Dr. Mallikaarjun:

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

Name of Drug Product: Abilify®, aripiprazole, 2 mg, 5 mg, 10 mg, 15 mg, 20 mg, and 30 mg tablets

NDA Number: 21-436

Supplement number: S-004

Date of supplement: July 2, 2003

Date of receipt: July 3, 2003

This supplemental application was submitted as a "Supplement - Changes Being Effected in 30 days." The appropriateness of reporting the proposed change(s) as changes being effected in 30 days is under review.

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on September 1, 2003 in accordance with 21 CFR 314.101(a).

All communications concerning this supplement should be addressed as follows:

U.S. Postal Service:
Center for Drug Evaluation and Research
Division of Neuropharmacological Drug Products, HFD-120
Attention: Division Document Room, 4008
5600 Fishers Lane
Rockville, Maryland 20857

NDA 21-436/S-004

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Courier/Overnight Mail:

Food and Drug Administration

Center for Drug Evaluation and Research

Division of Neuropharmacological Drug Products, HFD-120

Attention: Document Room #4008

1451 Rockville Pike

Rockville, Maryland 20852

Center for Drug Evaluation and Research

If you have any question, please contact Mr. Steven Hardeman, R.Ph., Regulatory Management Officer, at (301) 594- 5525.

Sincerely yours,

Thomas F. Oliver, 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

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/s/

Thomas Oliver
8/5/03 06:32:44 AM