CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

74803

CHEMISTRY REVIEW(S)

1. CHEMISTRY REVIEW NO. 7

2. ANDA # 74-803

3. NAME AND ADDRESS OF APPLICANT

Barr Laboratories, Inc.
2 Quaker Road
P.O. Box 2900
Pomona, New York 10970-051

4. LEGAL BASIS FOR SUBMISSION

Prozac® 20 mg
Eli Lilly and Company
Lilly Corporate Center
Indianapolis, Indiana 46258

The drug substance is currently covered by two U.S. patents; #4314081, expiration date 2/2/01 and #4626549, expiration date 12/2/03. The applicant filed a Paragraph IV Certification and notified the innovator as required. The innovator has filed an action for patent infringement (4/10/96) and requested that approval not be made effective until at least the expiration of the thirty-month period provided by 21 USC ' 355(j)(4)(B)(iii), subject to an appropriate ruling by the court.

5. SUPPLEMENT(s) N/A

6. PROPRIETARY NAME

N/A

7. NONPROPRIETARY NAME

Fluoxetine Hydrochloride USP

8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A

9. AMENDMENTS AND OTHER DATES:

Firm:

12/9/95	Original submission.
2/22/96	New Correspondence - Submission of additional copies of analytical methods.
3/13/96	New Correspondence - Paragraph IV Notification Certification.
3/14/96	New Correspondence - Addendum to 3/13/96 correspondence.
6/15/98	Amendment - Response to Agency's letter of 7/9/96.
8/18/98	Bioequivalence Amendment.

4/12/99	Amendment - Response to Agency's letter of 3/12/99.
5/21/99	Telephone Amendment.
6/7/99	Telephone Amendment.
7/23/99	New Correspondence.
3-7-2k	Minor amendment, later withdrawn
3-17-2k	Minor amendment with withdrawn 3-7-2k amendment
4-18-2k	Telephone amendment
5-22-01	Minor amendment
7-19-01	Labeling amendment

FDA:

2/21/96	Receipt acknowledged.
4/17/96	Notification of Filing of Legal Action for Patent Infringement from innovator.
6/10/96	Issuance of Bioequivalence Deficiency letter.
7/9/96	Issuance of Not Approvable letter.
3/12/99	Issuance of Not Approvable facsimile.
3-15-2k	request to withdraw 3-7-2k amendment
4-5-2k	Telephone NA letter

10. PHARMACOLOGICAL CATEGORY

Antidepressant

11. Rx or OTC

Rx

12. RELATED IND/NDA/DMF(s)

DMF
DMF
DMF
DMF
DMF
DMF

13. DOSAGE FORM

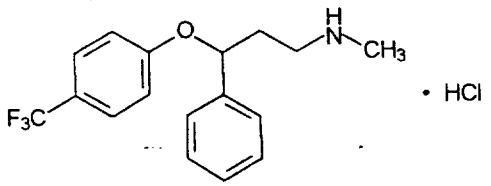
Hard Gelatin Capsule
for oral administration

14. POTENCIES

10 mg, 20 mg

15. CHEMICAL NAME AND STRUCTURE

Fluoxetine Hydrochloride
$C_{17}H_{18}F_3NO.HCl$; M.W. = 345.79



(")-*N*-Methyl-3-phenyl-3-[(α,α,α-trifluoro-*p*-toly)oxy]propylamine monohydrochloride. CAS [59333-67-4]

16. RECORDS AND REPORTS

5/15/96 - Bioequivalency review, Z. Wahba.
5/20/96 - Chemistry review #1, G.J. Smith.
6/17/96 - Labeling review, C. Hoppes.
8/18/98 - Labeling review, A. Vezza.
8/21/98 - Bioequivalency review, Z. Wahba.

17. COMMENTS

The ANDA was Tentatively Approved on 6-14-2000. Firm provides the following changes in the minor amendment dated 5/22/01: site changes, test method and specification changes, manufacturing and packaging changes, and labeling changes before the final approval.

Status:

a. EER status: Pending

EER was requested for Barr , by B. McNeal on July 18, 2001 and found acceptable on July 24, 2001 for the control testing laboratory. However, an inspection is scheduled for August for the site as a finished dosage packager, labeler and stability tester. Pat Beers-Block sent an E-Mail to EES questions on 7/30/01 asking that the inspection be cancelled.

b. Method Validation status:

Methods validation not required since drug substance and product are compendial.

c. Bio-review status: Satisfactory

The Division of Bioequivalence found the 20 mg drug product equivalent to RLD and granted waiver for the 10 mg product.

d. Labeling review status: Satisfactory
Satisfactory per A. Vezza reviewed on 7-30-01.

e. DMF Satisfactory

DMF was reviewed and found satisfactory per L. Tang reviewed on 5-16-2000.

18. CONCLUSIONS AND RECOMMENDATIONS

Approval

19. REVIEWER: DATE COMPLETED:

Lucia C. Tang 7-25-2001

AUG 2 1999

Chemistry Comments to be Provided to the Applicant

AADA/ANDA: 74-803 APPLICANT: Barr Laboratories

DRUG PRODUCT: Fluoxetine HCl Capsules USP, 10 mg & 20 mg

The deficiencies presented below represent MINOR deficiencies.

Reference is also made to your amendments dated June 6, 1997; April 29, June 15, and August 18, 1998; April 12, April 30, May 14, May 21, and June 7, 1999, and your correspondence dated July 23, 1999.

Review of the data submitted in your correspondence dated July 23, 1999 shows that your drug product fails to meet compendial specifications through the proposed expiry dating when the amounts of Impurity I ((±) 1-Phenyl-3-methylamino-1-propanol) are included in the determination of Individual and Total Impurities. Please submit stability data demonstrating conformance to compendial requirements in support of the proposed 24 month expiration date.

Sincerely yours,

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research