CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75465

CHEMISTRY REVIEW(S)

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Generic Drugs
Abbreviated New Drug Application Review

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1. **CHEMISTRY REVIEW NO.** 5

2. **ANDA #** 75-755

3. **NAME AND ADDRESS OF APPLICANT**
Alphapharm Pty. Ltd.
15 Garnet Street
Carole Park, 4300, Qld.
Queensland 4300
Australia

U.S. Agent:
King and Spalding
1730 Pennsylvania Avenue, N.W.
Washington D.C. 20006-4706

4. **LEGAL BASIS FOR SUBMISSION**
The RLD is Prozac Tablets, 10 mg, manufactured by Eli Lilly Co. A citizen petition was filed for Fluoxetine Tablets 20 mg. U.S. Patent No. 4314081 expires on 2/2/2001, and U.S. Patent No. 4626549 expires on 12/2/2003. Pediatric Exclusivity ends on 8/2/01 (5/18/01).

A paragraph IV patent certification is appended. Updated patent certification and exclusivity Statement are provided on pp. 23-24, 4/26/01 and pp. 4, 5/18/01 respectively.

5. **SUPPLEMENT(s)**
N/A

6. **PROPRIETARY NAME**
N/A

7. **NONPROPRIETARY NAME**
Fluoxetine Tablets

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

9. **AMENDMENTS AND OTHER DATES:**
Firm:
12/6/1999 - Original Submission
1/21/2000 - Amendment
2/11/2000 - Correspondence
9/8/2000 - Amendment
3/16/00 - Amendment

7/12/01 - Amendment

FDA:
2/4/2000 - Receipt Acknowledged
6/16/2000 - Deficiency Letter
3/6/00 - T-con
6/29/01 - Tentative Approval

10. **PHARMACOLOGICAL CATEGORY**
Antidepressants

11. **Rx or OTC**
Rx

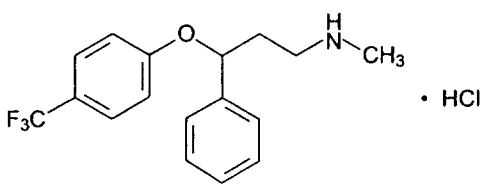
12. **RELATED IND/NDA/DMF(s)**
NDA - 20974
DMF
DMF
DMF
DMF
DMF
DMF
DMF
DMF
DMF
DMF
DMF

13. **DOSAGE FORM**
Tablets for
Oral Administration

14. **POTENCIES**
10 mg and 20 mg

15. **CHEMICAL NAME AND STRUCTURE**

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



Chemical Name:
a. Benzenepropanamine, *N*-methyl-γ-[4-(trifluoromethyl)phenoxy]-, hydrochloride, (±)-
b. (±)-N-Methyl-3-Phenyl-3-[(α,α,α-trifluoro-*p*-tolyl)oxy]propylamine hydrochloride

CAS-59333-67-4

16. **RECORDS AND REPORTS**

2/24/00 - Labeling Rev.
3/9/00 - Bioavailability/Bioequivalence Rev.#1
6/14/00 - Chemistry Rev.
6/26/00 - Submit Method Validation Request
8/28/00 - Method Validation Report
9/21/00 - Labeling Rev.
1/31/01 - Bioavailability/Bioequivalence Rev.#2
2/15/01 - Labeling Rev.
5/26/01 - Labeling Rev.
7/10/01 - Chemistry Rev.
8/1/01 - Chemistry Rev.

17. **COMMENTS**

Bioavailability/Bioequivalence studies are found satisfactory, 2/2/01.

Method Validation is satisfactory per Northeast Regional Laboratory, 8/28/00.

Changes in the tests and specifications for the drug substance raw material and finished drug products are not proposed (amendment dated 7/12/01).

18. **CONCLUSIONS AND RECOMMENDATIONS**

Recommend approval letter to issue.

19. **REVIEWER:** Tao Chin Wang
For Edwin Ramos

DATE COMPLETED: 8/1/01

Food and Drug Administration
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1. **CHEMISTRY REVIEW NO.** 2,3

2. **ANDA #** 75-755

3. **NAME AND ADDRESS OF APPLICANT**

Alphapharm Pty. Ltd.
15 Garnet Street
Carole Park, 4300, Qld.
Queensland 4300
Australia

U.S. Agent
King and Spalding
1730 Pennsylvania Avenue, N.W.
Washington D.C. 20006-4706
Tel: 202-737-0500
Fax: 202-626-3737

4. **LEGAL BASIS FOR SUBMISSION**

The reference listed drug is Prozac Tablets, 10 mg, manufactured by Eli Lilly and Company. A citizen petition was filed for Fluoxetine Tablets 20 mg. U.S. Patent No. 4314081 expires on 2/2/2001, and U.S. Patent No. 4626549 expires on 12/2/2003. There is no unexpired exclusivity for this product.

The firm files a paragraph IV patent certification.

5. **SUPPLEMENT(s)**

N/A

6. **PROPRIETARY NAME**

N/A

7. **NONPROPRIETARY NAME**

Fluoxetine Tablets

8. **SUPPLEMENT(s) PROVIDE(s) FOR:**

N/A

9. **AMENDMENTS AND OTHER DATES:**

Firm:

12/6/1999 -	Original Submission
1/21/2000 -	Amendment
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9/8/2000 -	Amendment

3/16/00 - Amendment

FDA:
2/4/2000 - Receipt Acknowledged
6/16/2000 - Deficiency Letter
3/6/00 - T-con

10. **PHARMACOLOGICAL CATEGORY**
Antidepressants

11. **Rx or OTC**
Rx

12. **RELATED IND/NDA/DMF(s)**
NDA - 20974
DMF
DMF
DMF
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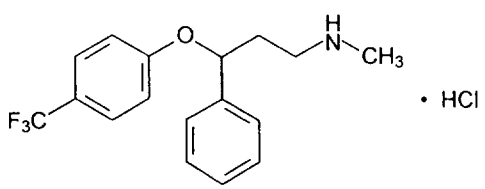

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a. Benzenepropanamine, *N*-methyl-γ-[4-(trifluoromethyl)phenoxy]-, hydrochloride, (±)-
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CAS-59333-67-4

16. **RECORDS AND REPORTS**

2/24/00 - Labeling Rev. #1
3/9/00 - Bioavailability/Bioequivalence Rev.#1

6/26/00 - Submit Method Validation Request
8/28/00 - Method Validation Report
9/21/00 - Labeling Rev. #2
1/31/01 - Bioavailability/Bioequivalence Rev.#2
2/15/01 - Labeling Rev. #3
3/26/01 - Labeling Rev. #4

17. **COMMENTS**

This application represents the first generic for these drug products.

Bioavailability/Bioequivalence studies are found satisfactory, 2/2/01.

DMF is adequate, 10/26/00.

Labeling is satisfactory, 3/26/01.

Acceptable EIR was issued by the Office of Compliance, 8/8/2000.

Method Validation is satisfactory per Northeast Regional Laboratory, 8/28/00.

18. **CONCLUSIONS AND RECOMMENDATIONS**

Minor Deficiency

19. **REVIEWER:** Tao-Chin L. Wang **DATE COMPLETED:** 3/29/2000

1. **CHEMISTRY REVIEW NO.** 1

2. **ANDA #** 75-755

3. **NAME AND ADDRESS OF APPLICANT**

Alphapharm Pty. Ltd.
15 Garnet Street
Carole Park, 4300, Qld.
Australia

U.S. Agent
Par Pharmaceutical Inc.
Attn: Dr. Robert Femia
One Ram Ridge Road
Spring Valley, New York 10977
Tel: 914-573-5708

4. **LEGAL BASIS FOR SUBMISSION**

The reference listed drug is Prozac Tablets, 10 mg, manufactured by Eli Lilly and Company. A citizen petition was filed for Fluoxetine Tablets 20 mg. U.S. Patent No. 4314081 expires on 2/2/2001, and U.S. Patent No. 4626549 expires on 12/2/2003. There is no unexpired exclusivity for this product.

The firm files a paragraph IV patent certification.

5. **SUPPLEMENT(s)**

N/A

6. **PROPRIETARY NAME**

N/A

7. **NONPROPRIETARY NAME**

Fluoxetine Tablets

8. **SUPPLEMENT(s) PROVIDE(s) FOR:**

N/A

9. **AMENDMENTS AND OTHER DATES:**

Firm:
12/6/1999 - Original Submission
1/21/2000 - Amendment
2/11/2000 - Correspondence

FDA:
2/4/2000 - Receipt Acknowledged

10. **PHARMACOLOGICAL CATEGORY**

Antidepressants

11. **Rx or OTC**

Rx

12. **RELATED IND/NDA/DMF(s)**

NDA - 20974
DMF
DMF
DMF
DMF
DMF
DMF
DMF
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DMF
DMF

13. **DOSAGE FORM**

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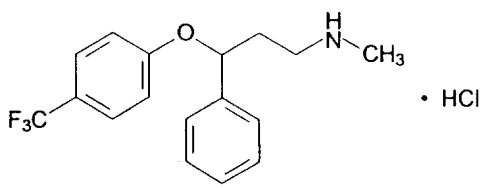

Chemical Name:

a. Benzenepropanamine, *N*-methyl-γ-[4-(trifluoromethyl)phenoxy]-, hydrochloride, (±)-.
b. (±)-N-Methyl-3-Phenyl-3-[(α,α,α-trifluoro-*p*-tolyl)oxy]propylamine hydrochloride.

CAS-59333-67-4.

16. **RECORDS AND REPORTS**

DMF is deficient.
Labeling in not satisfactory per A. Vezza, 2/24/00.
Bioavailability/Bioequivalence review (3/9/2000):

For Fluoxetine Tablets, 10 mg:
Dissolution specification revision requested.

For Fluoxetine Tablets, 20 mg:
The firm's in-vivo studies waiver request is denied.

Method validation for the drug products will be requested. EER result is pending.

17. **COMMENTS**
This application represents the first generic for these drug products.

Synthesis, Raw Material Controls, Container/Closure, Laboratory Controls are not Satisfactory.

18. **CONCLUSIONS AND RECOMMENDATIONS**
Not Approvable - Major

19. **REVIEWER:** Tao-Chin L. Wang **DATE COMPLETED:** 4/28/2000

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Generic Drugs
Abbreviated New Drug Application Review

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1. **CHEMISTRY REVIEW NO.** 4

2. **ANDA #** 75-755

3. **NAME AND ADDRESS OF APPLICANT**

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15 Garnet Street
Carole Park, 4300, Qld.
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Tel: 202-737-0500
Fax: 202-626-3737

4. **LEGAL BASIS FOR SUBMISSION**

The reference listed drug is Prozac Tablets, 10 mg, manufactured by Eli Lilly and Company. A citizen petition was filed for Fluoxetine Tablets 20 mg. U.S. Patent No. 4314081 expires on 2/2/2001, and U.S. Patent No. 4626549 expires on 12/2/2003. Pediatric Exclusivity ends on 8/2/01 (5/18/01).

The firm files a paragraph IV patent certification. Updated patent certification and exclusivity Statement are provided on pp. 23-24, 4/26/01 and pp. 4, 5/18/01 respectively.

5. **SUPPLEMENT(s)**

N/A

6. **PROPRIETARY NAME**

N/A

7. **NONPROPRIETARY NAME**

Fluoxetine Tablets

8. **SUPPLEMENT(s) PROVIDE(s) FOR:**

N/A

9. **AMENDMENTS AND OTHER DATES:**

Firm:
12/6/1999 - Original Submission

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FDA:
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3/6/00 - T-con

10. **PHARMACOLOGICAL CATEGORY**
Antidepressants

11. **Rx or OTC**
Rx

12. **RELATED IND/NDA/DMF(s)**
NDA - 20974
DMF
DMF
DMF
DMF
DMF
DMF
DMF
DMF
DMF
DMF
DMF

13. **DOSAGE FORM**
Tablets for
Oral Administration

14. **POTENCIES**
10 mg and 20 mg

15. **CHEMICAL NAME AND STRUCTURE**

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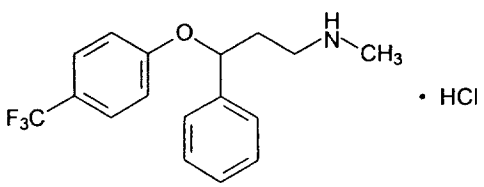

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b. (±)-N-Methyl-3-Phenyl-3-[(α,α,α-trifluoro-*p*-tolyl)oxy]propylamine hydrochloride

CAS-59333-67-4

16. **RECORDS AND REPORTS**

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9/21/00 - Labeling Rev.
1/31/01 - Bioavailability/Bioequivalence Rev.#2
2/15/01 - Labeling Rev.
3/26/01 - Labeling Rev.
4/10/01 - Chemistry Rev.

17. **COMMENTS**

Bioavailability/Bioequivalence studies are found satisfactory, 2/2/01.

DMF is adequate, 10/26/00.

Labeling is satisfactory, 5/8/01.

Acceptable EIR was issued by the Office of Compliance, 8/8/2000.

Method Validation is satisfactory per Northeast Regional Laboratory, 8/28/00.

18. **CONCLUSIONS AND RECOMMENDATIONS**

Tentatively Approvable

19. **REVIEWER:** Tao-Chin L. Wang **DATE COMPLETED:** 6/12/01