CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75465

CORRESPONDENCE

ANDA 75-465

JUN 26 2001

Reddy - Cheminor Inc.
U.S. Agent for Dr. Reddy's Laboratories Limited
Attention: Paul V. Campanelli
66 South Maple Avenue
Ridgewood, New Jersey 07460

Dear Sir:

This is in reference to your abbreviated new drug application dated September 24, 1998, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Fluoxetine Capsules USP, 10 mg, 20 mg and 40 mg.

Reference is also made to your amendments dated March 30 and September 26, 2000; and February 5, March 8, March 30, and May 25, 2001.

We have completed the review of this abbreviated application and have concluded that, based upon the information you have presented to date, the drug is safe and effective for use as recommended in the submitted labeling. Therefore, the application is **tentatively approved.** This determination is based upon information available to the Agency at this time, (i.e., information in your application and the status of current good manufacturing practices of the facilities used in the manufacturing and testing of the drug product) and is therefore subject to change on the basis of new information that may come to our attention.

The listed drug product (RLD) referenced in your application, Prozac® Capsules of Eli Lilly and Company, is currently subject to periods of patent protection which expire on August 2, 2001 (U.S. Patent No. 4,314,081 [the '081 patent]) and June 2, 2004 (U.S. Patent 4,625,549 [the '549 patent]). Your application contains a Paragraph III Certification under Section 505(j)(2)(A)(vii)(III) of the Act to the '081 patent stating that you will not market this drug product prior to the expiration of this patent. Your application also contains a Paragraph IV Certification and a Method of Use Statement under Section 505(j)(2)(A)(vii)(IV) and Section 505(j)(2)(A)(viii) of the Act

to the '549 patent. However, litigation is underway in the United States District Court for the Southern District of Indiana, Indianapolis Division involving a challenge to the patent (Eli Lilly and Company v. Cheminor Drugs, Ltd. and Reddy-Cheminor, Inc., Civil Action No. IP99-0024 C B/S). Therefore, final approval cannot be granted until:

1. a. the expiration of the 30-month period provided for in section 505(j)(5)(B)(iii) since the date of receipt of the 45-day notice required under section 505(j)(2)(B)(i), unless the court has extended or reduced the period because of the failure of either party to reasonably cooperate in expediting the action, or,

   b. the date of court decision [505(j)(5)(B)(iii)(I), (II), or (III)], which has been interpreted by the Agency to mean the date of the final order or judgement of that court from which no appeal can be or has been taken, or,

   c. the patent has expired, and

2. The Agency is assured there is no new information that would affect whether final approval should be granted.

We also note that should the patent litigation be resolved in favor of Cheminor Drugs, Ltd. and Reddy-Cheminor, Inc. prior to the expiration of the '081 patent which is the subject of a Paragraph III Certification, final approval of this application may not be made effective pursuant to 21 U.S.C. 355(j)(5)(B)(ii) of the Act until the '081 patent has expired, currently August 2, 2001.

Because the Agency is granting a tentative approval for this application, please submit an amendment at least 60-days (but not more than 90-days) prior to the date you believe your application will be eligible for final approval. This amendment should identify changes, if any, in the conditions under which the drug product was tentatively approved, and should include updated information such as final-printed labeling, chemistry, manufacturing and controls data, as appropriate. This amendment also serves to reactivate this application prior to final approval and should be submitted even if none of these changes were made since the date of this tentative approval letter. This amendment should be designated clearly in your cover letter as a MINOR AMENDMENT. With respect to the patent issues noted

above, this amendment should also provide information such as a copy of a final order or judgement from the court, a notice of a settlement agreement between the parties, a licensing agreement between you and the patent holder, or any other relevant information as appropriate to address these unexpired patents.

In addition to this amendment, the Agency may request at any time prior to the date of final approval that you submit an additional amendment containing the information described above. Failure to submit either or, if requested, both amendments may result in rescission of the tentative approval status of your application, or may result in a delay in the issuance of the final approval letter.

Any significant changes in the conditions outlined in this abbreviated application as well as changes in the status of the manufacturing and testing facilities' compliance with current good manufacturing practices (CGMPs) are subject to Agency review before final approval of the application will be made.

Please note that this drug product may not be marketed without final Agency approval under Section 505 of the Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under Section 501 of the Act and 21 U.S.C. 331(d). Also, until the Agency issues the final approval letter, this drug product will not be deemed approved for marketing under 21 U.S.C. 355 and will not be listed in the "Approved Drug Products with Therapeutic Equivalence Evaluations" list (the "Orange Book"), published by the Agency. Should you believe that there are grounds for issuing the final approval letter prior to June 2, 2004, you should amend your application accordingly.

At the time you submit any amendments, you should contact Bonnie McNeal, Project Manager, at 301-827-5849, for further instructions.

Sincerely yours,

/S/ 6/26/04

Gary Buehler
Acting Director
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 75-465

AUG 2 2001

Reddy-Cheminor Inc.
U.S. Agent for Dr. Reddy's Laboratories Limited
Attention: Paul V. Campanelli
66 South Maple Avenue
Ridgewood, New Jersey 07460

Dear Sir:

This is in reference to your abbreviated new drug application dated September 24, 1998, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Fluoxetine Capsules USP, 10 mg, 20 mg and 40 mg.

Reference is also made to the Tentative Approval letter issued on June 26, 2001 and to your amendments dated June 19, July 18 and 30, 2001.

The listed drug product referenced in your application is subject to a period of pediatric exclusivity which expires August 2, 2001. In addition the listed drug product is subject to a period of patent protection which expires June 2, 2004, (U.S. Patent No. 4,626,549 [the '549 patent]). Your application contains a Paragraph IV Certification and a Method of Use Statement under Section 505(j)(2)(A)(vii)(IV) and Section 505(j)(2)(A)(viii)of the Act to the '549 patent. You informed us that Eli Lilly and Company initiated a patent infringement action against you for your Paragragh IV Certification on the challenged claim in United States District Court for the Southern District of Indiana, Indianapolis Division (Eli Lilly and Company v. Cheminor Drugs, Ltd. and Reddy-Cheminor, Inc., Civil Action No. IP99-0024 C B/S). You have also notified us that you prevailed on one claim of the '549 patent in both the district court and in the court of appeals and made a Method of Use Statement to another claim.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. However, because of the unique (split) 180-day generic drug exclusivity issues

associated with this drug product, the Agency is prohibited from approving all three strengths at this time. **Thus, only the 40 mg strength of the drug product is approved at this time. The 10 mg and 20 mg strengths shall remain tentatively approved** and will not receive final approval until the remaining 180 days of exclusivity has expired. The Division of Bioequivalence has determined your Fluoxetine Capsules USP, 40 mg to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Prozac® Capsules, 40 mg of Eli Lilly and Company). Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application.

With respect to 180-day generic drug exclusivity and its impact on the approvability of the various strengths presented in this application, we note that Dr. Reddy's Laboratories Limited (Dr. Reddy's) was the first to submit a substantially complete ANDA with a Paragraph IV Certification for the 40 mg strength only. Therefore, Dr. Reddy's is eligible for 180-days of market exclusivity for the 40 mg strength. Subsequent applications for the 40 mg strength will be eligible for final approval not earlier than one hundred and eighty days after:

(1) the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application, or

(2) the date of a decision of a court in action described in clause (ii) holding the patent which is the subject of the certification to be invalid or not infringed, whichever is earlier [Section 505(j)(B)(iv)].

If you have any questions concerning the effective date of approval of an abbreviated new drug application and the Agency's elimination of the requirement that an ANDA applicant successfully defend a patent infringement suit to be eligible for 180-days of marketing exclusivity, please refer to the interim rule published in the November 5, 1998 Federal Register (Volume 63, No. 214, 59710).

We are unable to grant final approval to the 10 mg and 20 mg strengths at this time because abbreviated applications for Fluoxetine Capsules USP, 10 mg and 20 mg, each containing a Paragraph IV Certification for these strengths were accepted for filing by OGD prior to the filing of your application.

Subsequent applicants for the 10 mg and 20 mg strengths may not be approved earlier than one hundred and eighty days after:

(1) the date the Secretary recieves notice from the applicant under the previous application of the first commercial marketing, or

(2) the date of a decision of a court in action described in clause (ii) holding the patent which is the subject of the certification to be invalid or not infringed, whichever is earlier [Section 505(j)(5)(B)(iv)].

With respect to the "first commercial marketing" the Agency expects that you will begin commercial marketing of the 40 mg strength of this drug product in a prompt manner. Please submit correspondence to your application stating the date you commence commercial marketing of the 40 mg strength.

Under Section 506A of the Act, certain changes in the conditions described in this abbreviated application for the 40 mg strength require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application for the 40 mg strength are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of the 40 mg strength Fluoxetine Capsules USP.

We request that you submit, in duplicate, any proposed advertising or promotional copy, which you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-40). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-40) with a completed Form FD-2253 at the time of their initial use.

With respect to the continuation of the tentative approval status of the 10 mg and 20 mg strengths of this drug product, our decision is based upon information available to the Agency at this time (i.e., information in your application and the status of current good manufacturing practices (CGMPs) of the facilities used in the manufacture and testing of the drug product), and is subject to change on the basis of new information that may come to our attention.

To provide for final approval of the 10 mg and 20 mg strengths, please submit a supplemental application as directed below. The Agency will provide written notice of the information needed to determine the earliest possible final approval date of your supplemental application for the 10 mg and 20 mg strengths under section 505(j)(5)(B)(iv) as soon as such information becomes available. The supplemental application, which must be submitted for prior approval between 60 and 90 days prior to the date you believe these strengths will be eligible for final approval, should include updated information such as final-printed labeling, and chemistry, manufacturing and controls data as appropriate. Alternatively, a prior approval supplement should be submitted to request final approval of these strengths and stating that no changes have been made to the application since the date of this letter. Because of the unique circumstances associated with exclusivity for this drug product, the office will entertain your request that the supplemental application be granted "expedited review" status.

Any changes in the conditions outlined in this abbreviated application and the status of the manufacturing and testing facilities' compliance with current good manufacturing procedures are subject to Agency review before final approval of the supplemental application will be made.

In addition to, or instead of the supplemental application requesting final approval of the additional strengths, the Agency may at any time prior to final approval, request that you submit an informational document containing the information stated above.

Failure to submit the supplemental application or informational document may result in rescission of the tentative approval determination, or delay in issuance of the final approval letter for the 10 mg and 20 mg strengths.

The 10 mg and 20 mg strengths of Fluoxetine Capsules USP may not be marketed without final Agency approval under Section 505 of the Act. The introduction or delivery for introduction into interstate commerce of these unapproved strengths before the final approval date is prohibited under Section 501 of the Act. Also, until the Agency issues the final approval letter, the 10 mg and 20 mg strengths of the drug product will not be listed in the Agency's "Approved Drug Products with Therapeutic Equivalence Evaluations" list (the "Orange Book").

Should you have any questions about the approval status of the various strengths of drug product presented in your application, or about the timing or content of the supplemental application to provide for final approval of the remaining strengths, please contact Ms. Bonnie McNeal, Project Manager, at (301) 827-5849.

Sincerely yours,

/S/

Gary Buehler 8/2/01
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 75-465

Reddy-Cheminor, Inc.
Attention: Paul V. Campanelli
U.S. Agent for Cheminor Drugs Ltd.
66 South Maple Avenue
Ridgewood, NJ 07450

NOV 19 1998

Dear Sir:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

NAME OF DRUG: Fluoxetine Capsules USP, 10 mg and 20 mg

DATE OF APPLICATION: September 24, 1998

DATE (RECEIVED) ACCEPTABLE FOR FILING: September 25, 1998

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Tim Ames
Project Manager
(301) 827-5849

Sincerely yours,

/S/

Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

REDDY-CHEMINOR, INC. Rx-C

66 South Maple Avenue,
Ridgewood, NJ 07450
Phone: 201-444-4424
Fax: 201-444-1456

VIA HAND DELIVERY

July 30, 2001

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room, Room 150
Metro Park North II
7500 Standish Place
Rockville, MD 20855-2773

ORIG AMENDMENT

Reference: ANDA 75-465 Fluoxetine Capsules USP, 40 mg, 20mg and 10 mg
Minor Amendment

Request for Final ANDA Approval Subsequent to the
Final Non Appealable Judgment of the United States District Court in
Cause No. IP 01-442-CB/S, Consolidated Civil Action No. IP 98-1394 C-B/S
and Expiration of Patent Number 4,314,081

Dear Sir/Madam:

This correspondence is being provided by the US Agent, Reddy-Cheminor, Inc. on behalf of Dr. Reddy's Laboratories Limited, [redacted]epalli, India, 502 325. Dr. Reddy's Laboratories Limited is hereby submitting a [redacted]endment to the abbreviated new drug application ("ANDA") for Fluoxetine Capsules USP, 40 mg, 20 mg and 10 mg tentatively approved on June 26, 2001. Dr. Reddy's Laboratories is hereby requesting final approval of its Fluoxetine Capsules USP, 40 mg,-20 mg and 10 mg.

On or about January 11, 1999, Eli Lilly filed Civil Action No. 99-0024 C-B/S, relating to Dr. Reddy's Laboratories (formerly known as Cheminor Drugs Ltd.) ANDA for Fluoxetine Capsules, USP 10 mg and 20 mg. On May 3, 1999, that case was consolidated with cases involving Zenith-Goldline Pharmaceuticals and Teva Pharmaceuticals USA under Civil Action No. IP 98-1394 C-B/S.

On or about November 3, 1999, Eli Lilly filed a second complaint relating to Dr. Reddy's Laboratories (formerly known as Cheminor Drugs Ltd.) Fluoxetine Capsules USP, 40 mg, Civil Action No. 99-1697 C-B/S. On December 1, 1999, this second case was consolidated into Civil Action No. IP 98-1394 C-B/S.

On or about April 2, 2001, a third complaint was filed against Dr. Reddy's Laboratories (formerly known as Cheminor Drugs Ltd.) relating to Fluoxetine Tablets, 10 mg, Civil Action No. 01-0442 C-B/S. This third case was not consolidated.

On July 18, 2001, the Court of Appeals for the Federal Circuit denied Lilly's second combined petition for rehearing and rehearing en banc in Appeal Nos. 99-1262, -1264, and -1303; Eli Lilly and Company v. Barr Laboratories, Inc. Thereafter, Lilly asked the Federal Circuit to stay its mandate; however, Lilly's motion was denied and the Federal Circuit issued its mandate on July 26, 2001.

As a result of the Federal Circuit's decision regarding Barr Laboratories, the United States District Court, Southern District of Indiana, Indianapolis Division issued a Final Judgment on July 27, 2001, in the first and second action that had been consolidated under Civil Action No. IP 98-1394 and in the third case under Civil Action No. 01-0442. As reflected in those Final Judgments, copies of which are attached hereto, Eli Lilly agreed not to appeal the Final Judgments and the Court's Judgments therefore provide "this Judgment is a final Judgment from which no appeal has been or can be taken and the right to appeal lapses concurrently with entry hereof."

All three of Eli Lilly's complaints asserted patent infringement based on claims 6 and 7 of U.S. Patent Number 4,626,549. Judgment was entered in favor of defendants and against Eli Lilly on claims 6 and 7 of U.S. Patent Number 4,626,549 based on the Federal Circuit's finding of invalidity of claim 7 and the District Court's finding of claim preclusion arising from the Federal Circuit decision. Therefore, Lilly's patent infringement claims were dismissed with prejudice.

Thus, based on the issuance of a non-appealable Final Judgment by the District Court, we are submitting this minor amendment so that our ANDA for Fluoxetine Capsules USP, 40 mg, 20 mg and 10 mg can reach final approval.

Dr. Reddy's Laboratories intends to market Fluoxetine Capsules USP, 20 mg and 10mg upon the expiration of the period of 180-day market exclusivity afforded to another manufacturer who was the first to file paragraph IV certifications for those dosage strengths.

Further, Dr. Reddy's Laboratories will not market its Fluoxetine Capsules USP, 40 mg until after Patent Number 4,314,081's pediatric exclusivity extension expires on August 2, 2001.

Please be advised that there are no changes, other than those previously submitted with respect to labeling, in the conditions under which Fluoxetine Capsules USP, 40 mg, 20 mg and 10 mg was tentatively approved.

Based upon the information presented in this minor amendment, Dr. Reddy's Laboratories Limited hereby requests final approval of its application for Fluoxetine Capsules USP, 40 mg, 20 mg and 10 mg be granted.

This information is provided as a single volume in an archival copy and duplicate copy.

This concludes our minor amendment submission. We request that this information be reviewed expeditiously so that full approval of Dr. Reddy's ANDA may be granted as soon as possible.

Should you have any additional questions I can be contacted at (201) 444-4424.

Very truly yours,

REDDY-CHEMINOR, INC.

Paul V. Campanelli
Vice President, Formulations Business

Attachments

cc Duplicate Chemistry Jacket
Reddy-Cheminor File Copy
Dr. Reddy's Laboratories Limited File Copy

REDDY-CHEMINOR, INC. Rx-C

66 South Maple Avenue
Ridgewood, New Jersey 07450
Telephone (201) 444-4424
Telefax (201) 444-1456

Labeling review
drafted 5/16/00
A. Vega

May 9, 2000

NDA ORIG AMENDMENT
N/Ac

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Major Amendment

Reference : Fluoxetine Capsules, USP, 10 mg, 20 mg and 40 mg
ANDA 75-465

Dear Sir/ Madam:

This is in reference to your letter dated March 20, 2000 regarding our pending ANDA 75-465 for Fluoxetine Capsules, USP, 10 mg, 20 mg submitted on September 24, 1998 and subsequent Major Amendment to include Fluoxetine Capsules, USP, 40 mg filed on September 20, 1999. Reddy-Cheminor, Inc., US Agent for Cheminor Drugs Limited (CDL), herewith submits an amendment to the above referenced ANDA to include the following information in response to the Agency's comments:

A. **Chemistry Deficiencies:**

FDA Comment:

1) **Regarding Components and Composition:**

We note that empty hard gelatin capsule size "0" is used in the components and composition statement for the 40 mg strength. Please include the sizes for the 10 mg and 20 mg in the components and composition statement.

Response:

The components and composition statement of Fluoxetine Capsules USP, 10 mg and 20 mg have been revised to include the size of the empty hard gelatin capsules and are provided in *Exhibit I.*

FDA Comment

2) **We note that there is no potential Organic Volatile Impurities to be present in the manufacture of the drug substance. However, the specifications of Organic Volatile Impurities were listed in the drug substance. Please update your specifications for Organic Volatile Impurities in the drug substance (Fluoxetine Hydrochloride) and Pregelatinised Starch NF per USP 24 requirements and resubmit.**

Response:

The specifications for Organic Volatile Impurities in the drug substance (Fluoxetine Hydrochloride, USP) and Pregelatinized Starch,NF, have been updated as per USP 24 requirements and are provided in *Exhibit II.*

FDA Comment

3) **Regarding Gelatin Capsules:**

We note that the specifications on description of hard gelatin capsule shells for 10 mg (page 45 of September 14, 1999 amendment) and 20 mg (page 48 of September 14, 1999 Amendment) and 40 mg (page 339 of September 20, 1999 Amendment) is not acceptable. Please clearly identify the color, shape and printing and color of ink and resubmit.

Response:

The Specifications on description of hard gelatin capsule shells for Fluoxetine Capsules, USP 10 mg, 20 mg and 40 mg have been revised to identify the color, size, printing and color of ink. The revised specifications are provided in *Exhibit III.*

FDA Comment

4) **Submit the following information for the unit dose (e.g. blister) package:**
   i. **Light transmission test**
   ii. **Physico – chemical tests**
   iii. **Permeation tests**
   iv. **Acceptance specification**
   v. **Leak test**

Response:

i. Light Transmission Test

The packaging components used in the unit dose blisters for Fluoxetine Capsules, USP 40 mg are, PVC Film with Aclar (Base Film) and Aluminum Foil Paper backed peelable (Lidding Foil). Cheminor requests a waiver to perform the above tests due to following reasons:

- PVC Film with Aclar (Base Film): This blister component is not intended to be light resistant, as the unit dose blister card is packaged in an outer carton.

- Aluminum Foil Paper Backed Peelable: Aluminum Foil is an opaque material and due to the nature of Aluminum, it is impossible for the light to pass through the foil.

ii. *Physico – Chemical Tests*

- Physico – Chemical Tests have been included in the specifications for the Base Film (PVC Film with Aclar). The updated specifications and the test data are provided in *Exhibit IV.*

iii. *Permeation Tests*

- Permeation test data for the unit dose blisters as per USP <671> are provided in *Exhibit V.*

iv. Acceptance specification

- The Acceptance Specifications are provided in *Exhibit VI.*

v. Leak Test

- The leak test on unit dose blisters is performed as in-process test during blister packing operation. The data on the leak test for Fluoxetine Capsules, USP 40 mg have been provided in the Executed Batch Production Record page 602 and 604 of our Major Amendment dated 20th September, 1999. The procedure for leak test is provided in the General Test Procedure (GTP) No.: GP077-01. Please refer *Exhibit VII.*

FDA Comment

5) **We note that moisture content tests or loss on drying (LOD) tests have replaced brittleness tests in the stability studies. Please include the same tests in the finished product release specifications for each strength also.**

Response:

The finished product release specifications and test procedures of Fluoxetine Capsules, USP, 10 mg, 20 mg and 40 mg have been revised to include Loss on drying (LOD) of capsule shells and the Loss on drying (LOD) of contents of capsules. The revised finished product specifications and test procedures are provided in *Exhibit VIII.*

B. On March 30, 2000, Reddy-Cheminor, Inc., U.S. Agent for CDL, submitted a response to the Bioequivalence deficiencies contained in the Agency's fax dated November 24, 1999. This response did not require any chemistry, manufacturing and controls changes.

C. Labeling Deficiencies

Reddy-Cheminor, Inc., U.S. Agent for CDL, has modified the labeling in response to the Agency's comments and in accordance with the June, 1999 Drug Labeling Changes for PROZAC [June 16, 1999: Lilly] as obtained via the FDA Medical Products Reporting Program (http://www.fda.gov/medwatch). Four draft copies of the proposed labeling are supplied as follows: the bottle labeling for Fluoxetine Capsules, USP, 10 mg, 20 mg and 40 mg is included in *Exhibit IX*; the unit dose labeling for Fluoxetine Capsules, USP, 40 mg is included in *Exhibit* X; and the outsert labeling is included in *Exhibit XI*. In addition, a side-by-side comparison of the proposed labeling with the last submission with all differences annotated and explained is submitted in *Exhibit XII*.

Additional Information

In addition to the aforementioned responses to the deficiencies cited by the agency, Reddy-Cheminor, Inc., U.S. Agent for CDL, is taking this opportunity to include the following information in the ANDA:

1) The dissolution method has been revised as per USP 24, Supplement 1 in the test procedure for the finished product (release) of Fluoxetine Capsules, USP 10 mg, 20 mg and 40 mg. The dissolution parameters and specifications have not been revised. For revised finished product (release) specifications and test procedure, please refer to *Exhibit VIII*. Comparative dissolution data obtained from the previous finished product (release) dissolution test procedure and the USP 24, Supplement 1 test procedure is also included in Exhibit VIII.

Pursuant to 21 CFR 314.440(a)(4), a third copy of this application is enclosed. This is the required field copy and we certify that it is a true copy of the technical section as described in 21 CFR 314.50 (d)(1).

Included in this submission is an extra copy of our cover letter. Please acknowledge by date stamping this letter upon receipt and forwarding this copy to us in the self-addressed stamped envelope provided for your convenience.

Please contact the undersigned at (201) 444-4424 or by fax at (201) 444-1456 if you have any questions concerning this submission.

Sincerely,

Paul V Campanelli
Vice President, Formulations Business
Reddy-Cheminor Inc.
US Agent for Cheminor Drugs Limited

REDDY-CHEMINOR, INC.

66 South Maple Avenue
Ridgewood, New Jersey 07450
Telephone (201) 444-4424
Telefax (201) 444-1456

lyhelim review
drafted 11/15/99
A. Vezza

NDA ORIG AMENDMENT
N/AC

September 14, 1999

Office of Generic Drugs
Food and Drug Administration
Center for Evaluation and Research
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Major Amendment

Reference: Fluoxetine Capsules, USP, 10 mg and 20 mg
ANDA 75-465

Dear Sir/Madam:

This is in reference to your letters dated June 15, 1999 and July 28, 1999 regarding pending ANDA 75-465 for Fluoxetine Capsules, USP, 10 mg and 20 mg, submitted on September 24, 1998. Reddy-Cheminor, Inc., U.S. Agent for Cheminor Drugs Limited (CDL) is providing the following information in response to the Agency's correspondence:

A. Chemistry Deficiencies (June 15, 1999)

FDA Comment:

1. Regarding components and composition:

a. We note that Ferric Oxide black are present in the formulation of the 10 mg and 20 mg. Please provide the amount of iron oxide per capsule for the 10 mg and 20 mg capsule. This is required in order to comply with 21 CFR 1200 which limits the amount of elemental iron to not more than 5 mg per day.

b. Please include the empty capsule weight for each strength in the composition statement.

c. Submit the revised composition of the drug product based on the above comments.

Response: **1a.** Ferric Oxide Black (Iron Oxide Black) is present in the black printing ink used for the Fluoxetine Capsules, USP, 20 mg as described in the original ANDA in Section VIII, pages 3177 - 3187. Ferric Oxide Black is not present in the white printing ink used for the Fluoxetine Capsules, USP, 10 mg as described in the original ANDA in Section VIII, pages 3168 - 3175. Information provided on page 260 in Section VI of the ANDA erroneously implied that Ferric Oxide Black was used in the printing inks for both the 10 mg and 20 mg potencies. This page has been corrected to reflect the appropriate printing ink ingredients and is provided in Exhibit I.

CDL's formulations for Fluoxetine Capsules, USP, 10 mg and 20 mg are in compliance with 21 CFR § 73.1200(c) which restricts the amount of iron oxide ingested to not more than (NMT) 5 mg elemental iron per day. Please see Exhibit II for a summary of the maximum daily intake of iron for Fluoxetine Capsules, USP, 10 mg and 20 mg. Also included in Exhibit II is a letter from the capsule shell manufacturer, indicating the amount of elemental iron present in the ink used for printing the empty capsules for Fluoxetine Capsules, 20 mg.

1b. The Quantitative Statements of the Composition of the Drug Products have been revised to include the empty capsule weights and are provided in Exhibit III.

1c. The revised composition statements are included in Exhibit III.

FDA Comment:

2. Regarding gelatin capsules:

Submit the tests and specifications for imprinting inks. Also, provide information along with certification that the ink meets all the requirements of the indirect food additives regulation 21 CFR parts 174-178, 181 and 182.

Response: The empty capsule shells used in the manufacture of Fluoxetine Capsules, USP, 10 mg and 20 mg are imprinted by the capsule manufacturer, and then shipped to CDL.

The tests and specifications for the imprinting inks, obtained from the ink manufacturer, can be found on pages 3174 (white), 3184 (, black) and 3185 (black) of the original ANDA submission. The product specifications from the ink manufacturer certify that the ink ingredients meet the requirements listed in USP, F.C.C. or 21 CFR for the intended use in food and drugs.

Quantitative disclosures of the inks' contents can be found on pages 3175 white), 3186 black) and 3187 black). For your convenience copies of these pages are provided in Exhibit II.

FDA Comment:

3. The submission fails to provide a complete formula card and satisfactory batch records. In this regard:

a. Please provide the control limit of empty capsule weight variation, weight variation of filled capsule and content for each strength (pages 3311-3326 for 10 mg and pages 3389-3404 for 20 mg) in the blank batch records.

b. We note that in-process specifications for blend uniformity were provided as 90% to 110.0% with relative standard deviation not more than 6% (pages 3605 & 3634 of the original submission). However, we recommend blend uniformity analysis acceptance criteria as 90% to 110.0% (mean of individual test results) with a relative standard deviation (RSD) of NMT 5.0%.

c. Blend homogeneity testing should be specified for the production batches.

Response: 3a. At present, the average weight of the empty capsules is being checked during the release of the empty capsule shells and therefore weight variation of the empty capsules is not included in the manufacturing records. However, the Hard Gelatin Capsule Shells standard test specifications and method have been revised to include a test and control limit for weight variation of the empty

capsule shells and are provided in Exhibit IV. The empty capsule shell analysis reports, RC0046 (10 mg) and RC0047 (20 mg), were updated in compliance with the revised test method and are also included in Exhibit IV.

The limits for weight variation of the filled capsules and the capsule contents are provided in the text of the proposed commercial batch manufacturing records (10 mg: ANDA page 3306 and 20 mg: ANDA page 3384). In addition, the in-process check records included in these master manufacturing records have been revised to include product-specific information and the limits for weight variation and capsule contents (Exhibit V).

3b. The in-process specifications for Fluoxetine Capsule Blend have been revised to meet the criteria of 90.0% to 110.0% (mean of individual test results) with a relative standard deviation (RSD) of NMT 5.0%. Revised specifications for the 10 mg and 20 mg capsule blends are provided in Exhibit VI.

3c. CDL commits to perform Blend Uniformity testing on all production batches of Fluoxetine Capsules, USP, 10 mg and 20 mg. Please refer to the revised sampling/testing protocol plans included in Exhibit VI.

FDA Comment:

4. We note that 85 cc HDPE and 950 cc HDPE bottles were used for packaging 30's, 100's and 1000's package size for Fluoxetine Capsules, 10 mg and 20 mg. However, 60 cc, HDPE bottle, 100 cc HDPE, 200 cc HDPE, 300 cc HDPE, 500 cc HDPE, 750 cc HDPE bottles were provided in Annexure-1 (Pages 3770-3782) for container diagrams. Please clarify use of those containers.

Response: Pages 3770 – 3781 are attachments to the Standard Test Procedure (STP) No. PP001-02 for High Density Polyethylene (HDPE) Containers, which is a common test procedure for all of the sizes of HDPE containers. The STP, along with all of the attachments, is included in the ANDA, even though some are not relevant for the present submission. Only the 85 cc and 950 cc HDPE bottles will be used to package these products, as described on pages 3697 – 3701 of the original ANDA.

FDA Comment:

5. **Submit the actual torque test for cap removal covering the 30's, 100's and 1000's capsules package sizes for each strength.**

Response: The actual torque test results for cap removal for the 30, 100 and 1000 capsule fill packages, for each strength, are included in Section XII of the original ANDA on the following pages:

Strength	Fill Count	Capacity	Page #
10 mg	30	85 cc	3523
	100	85 cc	3525
20 mg	30	85 cc	3578
	100	85 cc	3582
	1000	950 cc	3590

The Torque test operating instruction OI No. OPD057-00 is provided in Exhibit VII.

FDA Comment:

6. **Regarding the finished product:**

   a. **USP 23 Supplement 7 and COA of your finished product indicates that "not more than 0.25% of any individual impurity is found, and not more than 0.40% of total impurities is found" of drug product Chromatographic Purity. Please revise your related substances specifications in in-process testing in capsule filling stage to be consistent with current compendial requirements and your own finished product specifications and resubmit the COA in the capsule filling stage (see pages 2624, 4228, 4233, and etc.)**

   b. **Please provide complete description of drug product in the finished dosage form (pages 4228 & 4231) to be consistent with those in the stability protocol (pages 4285 & 4286).**

   c. **Please include brittleness tests in the finished dosage form and stability studies.**

Response: 6a. Chromatographic Purity testing is conducted on finished product samples for release and stability. In-process samples will not be tested for Chromatographic Purity for commercial production batches, however for the exhibit batches this in-process testing was performed. Pages 3624 and 3658 represent COAs for pooled

samples taken during the encapsulation stage. For commercial production batches, these samples would be considered as finished product release samples, however for these exhibit batches the samples were compared against the in-process specifications including Related Substances. At that time the Chromatographic Purity limits were NMT 0.25% for individual impurities and NMT 0.7% for total impurities. As Chromatographic Purity testing will not be performed for in-process samples for commercial batches, there are no revised specifications or in-process COAs to submit.

Two sets of finished product release COAs were submitted in the original ANDA for the exhibit batches. For the 10 mg product, one COA represents testing for the pooled sample taken during the encapsulation stage (Pages 3896 and 4228). At that time the Chromatographic Purity limits were NMT 0.3% for individual impurities and NMT 1.0% for total impurities. Subsequently, the specifications were revised as per USP 23, Supplement 7, the product was retested and a second COA was provided (Pages 3897-3898 and 4226-4227). Similarly, for the 20 mg product, one COA (Pages 3901 and 4233) represents testing conducted prior to USP 23 Supplement 7 and the second COA provided (Pages 3902-3903 and 4231-4232) represents the retest data.

6b. The post-approval stability protocol contains the capsule descriptions to be used for all commercial batches (Exhibit XII). The proposed imprint for production batches is as follows:

For 10 mg	Cap: FLUOXETINE 10 mg	Body: SHN
For 20 mg	Cap: FLUOXETINE 20 mg	Body: SHN

The finished product specifications have been revised to provide a complete description of the drug product to be consistent with the stability protocol and are provided in Exhibit VIII.

In addition, a complete description of the drug product in the finished dosage form has been provided on the revised analysis reports for Fluoxetine Capsules, USP, 10 mg and 20 mg which are also included in Exhibit VIII. Please note that the exhibit batches consist of capsules imprinted with "Capsugel" on the body and "Axial Print" on the cap, as explained on page 3165 of the original ANDA.

6c. Emptied capsule samples of Fluoxetine Capsules, 20 mg, from 21 months stability samples stored under controlled room temperature (CRT) conditions (25°C and 60% relative humidity), and emptied capsule samples of Fluoxetine Capsules, 10 mg, from 18 months CRT stability samples, were tested for loss on drying (LOD). As shown by the data included in Exhibit IX, the capsules did not undergo any significant loss in moisture content. Furthermore, accelerated and room temperature dissolution data were consistent and well within specification for all stability intervals tested. Updated stability reports are provided in Exhibit X. Capsugel, the manufacturer of the empty capsule shells, could not recommend a specific test for brittleness, but suggested using LOD testing, as moisture loss is the best indicator of brittleness. Therefore, we are proposing LOD specifications for capsule contents and capsule shells for the finished dosage form stability studies. The revised stability specifications for Fluoxetine Capsules, USP, 10 mg and 20 mg and the standard test procedures are included in Exhibit XI.

FDA Comment:

7. **Your application fails to contain a satisfactory stability protocol and supporting stability data. In this regard:**

   a. **Please include composition of the drug product in stability report.**

   b. **Please include brittleness tests in the stability studies.**

   c. **We note that the descriptions of the drug product in the stability protocol (pages 4285-4286) is different from those in the stability data report (4292-4313). Please be consistent.**

   d. **On page 4291 you have explained your reason for not including moisture test and specification in the stability protocol. However, it is included in the stability data report. Capsules products are more susceptible to moisture. We strongly recommend that you include a test and specification for moisture in the stability protocol. Please revise and resubmit.**

Response: 7a. The composition of the drug product is included in the updated stability reports provided in Exhibit X.

7b. Please refer to our response to comment 6c. The stability

specifications and procedures for the finished product have been revised to include Loss on Drying testing for empty capsules and capsule contents and are included in Exhibit XI.

7c. As noted in our response to comment 6b, the capsule shell descriptions in the stability protocol for the commercial batches differ from the descriptions in the stability data reports because the capsules used for the exhibit batches, for which the stability data is submitted, were imprinted with different text. The description provided in the post-approval protocol reflects the imprint that will be used for commercial batches.

7d. The stability protocols have been revised to include moisture (Loss on Drying) testing of capsule contents and empty capsule shells (Exhibit XII).

FDA Comment:

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. You are advised that microbiological testing should be conducted on each lot of components, prior to use in the manufacture of the drug product, for those components for which the microbial limits test is specified by USP/NF [21 CFR 211.84 (d) (6)]. A 12-month retest period is recommended.

2. DMF has been reviewed and found deficient. A letter outlining the deficiencies has been sent to Dr. Reddy's Laboratories LTD. This ANDA cannot be approved until these deficiencies have been resolved.

Response: 1. Microbiological testing is conducted on Pregelatinized Starch and Empty Hard Gelatin Capsules as per the microbial limit test specified in USP/NF for every lot. Retesting is done after 12 months as per our retesting schedules.

2. A response to the deficiencies found in DMF was submitted to the Agency by Dr. Reddy's Laboratories Limited on July 6, 1999.

Bioequivalency Comments (June 15, 1999):

The following dissolution testing will need to be incorporated into your stability and quality control programs:

The dissolution testing should be conducted in 900 mL of water, at 37°C using USP Apparatus II (paddles) at 50 rpm. The test product should meet the following specifications:

Not less than % (Q) of the labeled amount of the drug in the dosage form is dissolved in 30 minutes.

Response:

The dissolution testing as described above has been incorporated into our release and stability testing requirements. Please refer to Exhibits VIII and XI.

Labeling Deficiencies (June 15, 1999 and July 28, 1999)

Response:

The container labels and package insert labeling for Fluoxetine Capsules, USP, 10 mg and 20 mg have been revised to correspond with the Agency's comments received on June 15, 1999 and July 28, 1999. Revised labeling, including 12 final printed copies and a side by side comparison of the proposed labeling with the labeling submitted in the previous submission, is included in Exhibit XIII.

Additional Information

In addition to the aforementioned responses to the deficiencies cited by the Agency, CDL is taking this opportunity to respond to an observation concerning the powder fineness specification for Fluoxetine Hydrochloride, USP, made during the FDA's inspection of Cheminor's facility in Bachepally, India on October 5-9, 1998. Cheminor Drugs Limited has revised the powder fineness and solubility specifications for the Fluoxetine Hydrochloride, USP drug substance used in the manufacture of Fluoxetine Capsules, USP, as follows:

Powder Fineness: Original ANDA

Amendment

Solubility: Original ANDA

Amendment

CDL's revised specifications and test procedure are provided in Exhibit XIV.

Dr. Reddy's Laboratories, manufacturer of Fluoxetine Hydrochloride, USP, drug substance, has amended their DMF to include the revised powder fineness specifications.

Pursuant to 21 CFR § 314.440(a)(4), a third copy of this amendment is also enclosed. This is the required field copy and we certify that it is a true copy of the technical section as described in 21 CFR § 314.50(d)(1).

Included in this submission is an extra copy of our cover letter. Please acknowledge by date stamping this letter upon receipt and forwarding this copy to us in the self-addressed stamped envelope provided for your convenience.

Please contact the undersigned at (201) 444-4424 or by fax at (201) 444-1456 if you have any questions concerning this submission.

Sincerely,

Paul V. Campanelli
Vice President, Formulations Business
Reddy-Cheminor, Inc.

U.S. Agent for Cheminor Drugs Limited

In closing, we acknowledge that the innovator 20-mg and 40-mg capsules are not weight proportional, however we believe that based on the data provided, a biowaiver for CDL's Fluoxetine HCl Capsules, 40-mg is supported. We respectfully request that the Agency reconsider our request for a waiver of *in vivo* bioavailability/bioequivalence study requirements for CDL's Fluoxetine HCl Capsules, USP 40-mg.

Included in this submission is an extra copy of our cover letter. Please acknowledge by date stamping this letter upon receipt and forwarding this copy to us in the self-addressed stamped envelope provided for your convenience.

Please contact the undersigned at (201) 444-4424 or by fax at (201) 444-1456 if you have any questions concerning this submission.

Sincerely,

Paul V. Campanelli
Vice President
Formulations Business
Reddy-Cheminor, Inc.

U.S. Agent for Cheminor Drugs Limited

cc: Jennifer Fan, Project Manager, Division of Bioequivalence, OGD (fax copy)
Dale Conner, Pharm.D., Director, Division of Bioequivalence, OGD (desk copy)

Labeling review drafted 7/25/01 A. Vega

REDDY-CHEMINOR, INC. Rx-C

66 South Maple Avenue,
Ridgewood, NJ 07450
Phone: 201-444-4424
Fax: 201-444-1456

HAND DELIVERED

July 18, 2001

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ORIG AMENDMENT
NDA

Reference: ANDA 75-465 Fluoxetine Capsules USP, 10, 20 and 40 mg
Minor Amendment: Labeling

Dear Sir/ Madam:

This submission is in reference to the Agency's Correspondence dated July 6, 2001 to our tentatively approved ANDA 75-465 for Fluoxetine Capsules, 10 mg, 20 mg and 40 mg. Reddy-Cheminor Inc., US Agent for Dr. Reddy's Laboratories Limited, here within submits a **Minor Amendment** to the above referenced ANDA to include the following information in response to the Agency's Comments.

A. Labeling Deficiencies:

FDA Comment:

1. GENERAL COMMENT

Please note that 12 copies of revised containers labels and insert labeling in FPL are required before full approval of this application. Submit the changes as explained in our 6-26-01 correspondence granting tentative approval for this application.

FDA Comments:

2. *INSERT*

a. *PRECAUTIONS*

i. *CNS Active Drugs – Decrease the prominence of the sub-section titles in this subsection ("Anticonvulsants" through "Sumatriptan") to be less than that of "CNS Active Drugs".*
ii. *Warfarin – "anticoagulant" and " coadministed" (delete hyphens)*
iii. *Geriatric Use – The title of this subsection should be in italics.*

b. *ADVERSE REACTION*

Other Events Observed in All U.S. Clinical Trials – The footnote beginning "Neuroleptic malignant..." should be the first footnote.

c. *HOW SUPPLIED*

Add the statement "Sarafem ™ is a trademark of Elly Lilly."

Response:

The Package Insert Leaflet (PIL) has been revised to include all the changes as recommended by the agency.

Twelve copies of the final printed labels (FPL) for the containers are provided in Section V.

Twelve copies each for the final printed inserts (10 mg, 20 mg, and 40 mg capsules combined) and also for 'only Fluoxetine Capsules, 40 mg' are provided in Section V.

A summary of changes is provided in Section IV.

Dr. Reddy's Laboratories Limited hereby declares that, since the time of tentative approval of our ANDA, we have not made any change in our application, except for the above referred response to the FDA labeling comments.

Please contact the undersigned at (410) 309-3145 or by fax at (410) 309-6145, if you have any questions concerning this submission.

Sincerely,

C. Jeanne Taborsky

C. Jeanne Taborsky
Regulatory Affairs

REDDY-CHEMINOR, INC. Rx-C

66 South Maple Avenue
Ridgewood, New Jersey 07450
Telephone (201) 444-4424
Telefax (201) 444-1456

May 1, 1998

NDA Catalogued 1/14/98

NEW CORRESP
NC

Mr. Tim Ames, Project Manager
Regulatory Support Branch
FDA-Office of Generic Drugs
MPN II, HFD-615
7500 Standish Place, Room 150
Rockville, MD 20855

RE: PATENT AMENDMENT
ANDA 75-465
Fluoxetine Capsules USP, 10 mg and 20 mg

Dear Mr. Ames:

In accordance with 21 CFR 314.95(b), we hereby certify that notice has been provided to each person identified under 314.95(a) and that notice met the content requirements under 314.95(c).

Further, in accordance with 21 CFR 314.95(e), enclosed please find documentation acknowledging receipt by Eli Lilly & Co. with respect to ANDA 75-465.

Please do not hesitate to contact us should you have any questions or require additional information.

With best regards,

REDDY-CHEMINOR, INC.

Paul V. Campanelli
Vice President, Formulations Business

Enclosure

cc: R. S. Prasad, Cheminor Drugs Ltd.

RECEIVED
DEC 07 1998
GENERIC DRUGS

Madhuri 12.7.98

Cheminor Drugs Limited

Pharma Division

Date: September 24, 1998

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Reference : **Fluoxetine Capsules, USP, 10 mg and 20 mg**
Abbreviated New Drug Application

Dear Sir/ Madam:

Cheminor Drugs Limited herewith submits an abbreviated new drug application (ANDA) for Fluoxetine Capsules, USP, 10 mg and 20 mg pursuant to Section 505 (j) of the Federal Food, Drug, and Cosmetic Act.

This ANDA refers to the listed drug, PROZAC® (Fluoxetine Hydrochloride) Capsules, 10 mg and 20 mg which is manufactured by Eli Lilly and Co., who is the holder of the approved application and which is listed in the 1998 Approved Drug Products with Therapeutic Equivalence Evaluations, 18th Edition. U.S Patent No.4,314,081 will expire on February 2,2001. U.S Patent No. 4,626,549 will expire on December 2, 2003. Cheminor Drugs Limited is not seeking to market the product until after the patents expire. The Exclusivity for the Indication for the treatment of Bulimia expires on November 21,1999. Cheminor Drugs Limited will not market the product with the Indication noted above until after the Market Exclusivity expires.

Fluoxetine Capsules, USP, 10 mg and 20 mg have been developed and will be manufactured, packaged and tested at Cheminor Drugs Limited, Via IDA Bollaram, Bachepalli - 502 325, INDIA in accordance with 21 CFR 210 and 211.

The manufacturer of the drug substance used to produce the ANDA batches of this product is Dr.Reddy's Laboratories, Hyderabad, INDIA, DMF No.

The required bioavailability / bioequivalence studies were conducted on Fluoxetine Capsules, USP, 20 mg and PROZAC® Capsules 20 mg by

These studies indicate that Fluoxetine Capsules, USP, 20 mg are bioequivalent to PROZAC® Capsules 20 mg.

The in-vitro dissolution profiles for Fluoxetine Capsules, USP, 10 mg and 20 mg are comparable to those of PROZAC® Capsules, 10 mg and 20 mg respectively. The 10 and 20mg formulations are proportionally similar therefore, a waiver of in-vivo bioavailability / bioequivalence study requirements for Fluoxetine Capsules, USP, 10 mg is requested.

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GENERIC DRUGS

September 24, 1998

Food and Drug Administration
Fluoxetine Capsules, USP, 10 mg and 20 mg
Abbreviated New Drug Application

Fluoxetine Capsules, USP, 10 mg and 20 mg are stable and a two year expiration dating is requested. The two year expiration dating for this product is supported by one, two and three months accelerated stability data (40°C ± 2°C / 75% ± 5% relative humidity) in the smallest and largest fill size of each container/closure system proposed for marketing.The stability studies were conducted under a stability protocol that is in conformance with the current FDA stability guidelines.

The dosage form, route of administration, active ingredient, potency and labeling (except DESCRIPTION,INDICATIONS AND USAGE and HOW SUPPLIED Sections) for Fluoxetine Capsules, USP, 10 mg and 20 mg are the same as those for PROZAC® Capsules, 10 mg and 20 mg.

This ANDA is submitted in thirteen volumes :

Volume I	:	Section I through Section V
Volume II through Volume IX	:	Section VI
Volume X	:	Section VII through Section XII
Volume XI	:	Section XI through Section XIII
Volume XII	:	Section XIV
Volume XIII	:	Section XV through Section XXI

Following this letter is a letter authorizing Reddy-Cheminor to act as the U.S agent for this ANDA. Included in this submission is an extra copy of our cover letter. Please acknowledge by date stamping this letter upon receipt and forwarding this copy to us in the self-addressed stamped envelope provided for your convenience.

Cheminor Drugs Limited
Pharma Division

September 24, 1998

Food and Drug Administration
Fluoxetine Capsules, USP, 10 mg and 20 mg
Abbreviated New Drug Application

Pursuant to 21 CFR 314.440 (a) (4), a third copy of this application is also enclosed.This is the required field copy and we certify that it is a true copy of the technical section as described in 21 CFR 314.50 (d) (1).

Sincerely,

Prakash V Mallya
Senior Manager-Regulatory Affairs

REDDY-CHEMINOR, INC.

66 South Maple Avenue
Ridgewood, New Jersey 07450
Telephone (201) 444-4424
Telefax (201) 444-1456

October 4, 1999

NEW CORRESP
NC

FDA-Office of Generic Drugs
Center for Drug Evaluation and Research
MPN II, HFD-615
7500 Standish Place, Room 150
Rockville, MD 20855

RE: PATENT AMENDMENT
ANDA 75-465
Fluoxetine Capsules, USP, 10 mg, 20 mg and 40 mg

Dear Sir or Madam:

In accordance with 21 CFR 314.95(b), Reddy-Cheminor, Inc., a subsidiary of Cheminor Drugs Ltd., is amending ANDA 75-465 for Fluoxetine Capsules, USP, 10 mg, 20 mg and 40 mg.

Reddy-Cheminor, Inc., hereby certifies that notice has been provided to each person identified under 314.95 (a) and that notice met the content requirements under 314.95 (c).

Further, in accordance with 21 CFR 314.95 (e) attached please find herewith documentation of receipt acknowledging receipt by Eli Lilly and Company, along with FDA 356h regarding ANDA 75-465.

Please do not hesitate to contact us if you have any questions or require additional information.

Very truly yours,
REDDY-CHEMINOR, INC.

Paul V. Campanelli
Vice President, Formulations Business
(US Agent for Cheminor Drugs Ltd.)

Attachments

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
OCT 05 1999
OGD

DR. REDDY'S
DR. REDDY'S LABORATORIES, INC.

ONE PARK WAY
UPPER SADDLE RIVER, NJ 07458
TELEPHONE (201) 760-2880
FAX (201) 760-0401

AUG 21 2001

NEW CORRESP
NC

SENT VIA FEDERAL EXPRESS

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Reference: ANDA # 75-465 Fluoxetine Capsules USP, 10 mg, 20mg, and 40 mg Correspondence

Dear Sir/ Madam:

Dr. Reddy's Laboratories, Inc. US Agent for Dr. Reddy's Laboratories Limited, Bachepalli 502 325, INDIA, is herein submitting a revised Letter of Authorization for US Agent with updated information.

Please be advised that the name and address of the US agent has changed.

Pursuant to *Code of Federal Regulations* Title 21 §314.440 (a) (4), a third copy of this communication is being provided. This is the required field copy and we certify that it is a true copy of the technical section as described in *Code of Federal Regulations* Title 21 §314.50 (d) (1).

This concludes our submission. Please contact C. Jeanne Taborsky at (410) 309-3145 or Paul V. Campanelli, Vice President Formulations Business, Reddy-Cheminor, Inc. at (201) 760-2880 ext 203, if you have any questions concerning this submission.

Sincerely yours,

C. Jeanne Taborsky

C. Jeanne Taborsky
Regulatory Affairs Consultant

CENTER FOR DRUG EVALUATION AND RESEARCH
RECEIVED
AUG 22 2001
OGD

DR. REDDY'S
Dr. Reddy's Laboratories, Inc.

ONE PARK WAY
UPPER SADDLE RIVER, NJ 07458
TELEPHONE: (201) 760-2880
FAX: (201) 760-0401

SENT VIA FEDERAL EXPRESS

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

JAN 16 2002

NEW CORRESP

Reference: ANDA 75-465 Fluoxetine Capsules USP, 10, 20, and 40 mg
Minor Amendment: Tentative to Final Approval

Dear Sir/ Madam:

Reddy-Cheminor Inc., US Agent for Dr. Reddy's Laboratories Limited, here within submits a Minor Amendment to the tentatively approved ANDA 75-465 for Fluoxetine Capsules, 10 mg, 20 mg and 40 mg. Reference is made to the Tentative Approval Letter dated

Please be reminded that the Firm had exclusivity to market the 40-mg strength. The FDA contacted the Firm on January 8, 2002 to advise that the exclusivity period will expire on January 29, 2002.

Dr. Reddy's Laboratories Inc. hereby warrantees that Dr. Reddy's Laboratories Limited has declares that, since the time of tentative approval of our ANDA, they have not made any changes to our application, except for the above referenced labeling additions. At the time that the Firm is prepared to market the 10 and 20 mg strength, they intend to submit the labeling change in the insert to the agency.

Please contact the undersigned at (410) 309-3145 or by fax at (410) 309-6145, if you have any questions concerning this submission.

Sincerely yours,

C. Jeanne Taborsky

C. Jeanne Taborsky
Regulatory Affairs

CENTER FOR DRUG EVALUATION AND RESEARCH
JAN 17 2002

NAI
G. Vezza
10/25/01
per P. Rickman:
OPDRA to take
action on this NC

DR. REDDY'S
Dr. Reddy's Laboratories, Inc.

ONE PARK WAY
UPPER SADDLE RIVER, NJ 07458
TELEPHONE: (201) 760-2880
FAX: (201) 760-0401

Office of Postmarketing Drug Risk Assessment
Center for Drug Evaluation and Research (HFD-400)
Food and Drug Administration
5600 Fishers Lane Room 15B-31
Rockville, MD 20857

OCT 15 2001

NC

NEW CORRESP

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

CENTER FOR DRUG EVALUATION AND RESEARCH
OCT 17 2001
OGD

Re: ANDA 75-465 Fluoxetine Capsules USP, 10, 20 and 40 mg
Date of Approval of 40 mg: August 02, 2001

Correspondence: Request for a Waiver for Reporting Anticipated Events in the Periodic Report

Dear Sir/Madam:

On behalf of Dr. Reddy's Laboratories Limited, Bachepalli, India; SciRegs, Regulatory Affairs for US Agent, Dr. Reddy's Laboratories Inc., is providing this correspondence. As requested, one copy is being submitted to the Office of Generic Drugs (OGD) and one copy is being submitted to the Office of Postmarketing Drug Risk Assessment. Reference is made to the Draft Guidance to Industry and prior communication with Min Chen and Peter Rickman regarding the format and content of this document.

In accordance with the provisions of *Code of Federal Regulations* Title 21 §314.80, Postmarketing reporting of adverse drug experiences and § 314.90 (a) Waivers, Dr. Reddy's Laboratories Limited here within requests a waiver for submission of FDA 3500As for individual case safety reports of nonserious, expected adverse experiences that, at a minimum, contain the four basis elements provided in the guidance as knowledge of:

- An identifiable patient
- An identifiable reported
- A suspect drug
- A nonserious anticipated adverse experience

DR. REDDY'S
Dr. Reddy's Laboratories, Inc.

Dr. Reddy's Laboratories Inc. commits to maintain records of these nonserious, expected adverse experiences in the corporate files both in the US and in India. Upon request from the agency, the Firm commits to provide copies of the reports within 5-calendar days after receipt of the request. The Firm will file information on the adverse experiences to the FDA in the summary tables section of the post marketing periodic report.

If you have any questions I can be reached by telephone at (410) 309-3145 or Fax at 410-309-6145 or Paul Campanelli can be contacted at 201 760-2990 extension 203 and by FAX at 201-760-0401.

Sincerely yours,

C. Jeanne Taborsky

C. Jeanne Taborsky
Regulatory Affairs

cc
Consumer Affairs: Salamandra
Paul Campanelli, Dr. Reddy's Laboratories Inc.
Pravir Choubey, Dr. Reddy's Laboratories Limited

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005-3315

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PALO ALTO
650•849•6600

WRITER'S DIRECT DIAL NUMBER:

TOKYO
011•813•3431•6943
BRUSSELS
011•322•646•0353

(202) 408-4068

January 27, 1999

VIA FEDERAL EXPRESS

Food & Drug Administration
Office of Generic Drugs
(HFD-600)
7500 Standish Place
Rockville, MD 20855

Re: Fluoxetine Hydrochloride Capsules, 10 and 20 mg
Abbreviated New Drug Application No. 75-465
Notification of Filing of Legal Action for Patent Infringement

Dear Sir or Madam:

We represent Eli Lilly and Company ("Lilly"), owner of United States Patent No. 4,626,549. We are sending you this letter on behalf of our client under 21 C.F.R. § 314.107(f)(2) to notify you of the following:

(1) Mr. Cameron Reid, President of Reddy-Cheminor, Inc. sent a letter to Lilly by certified mail on behalf of Reddy-Cheminor, Inc. and Cheminor Drugs, Ltd. (collectively, "Cheminor") stating that Cheminor was providing information pursuant to Section 505(j)(2)(B) of the Food, Drug and Cosmetic Act. The letter included the following information:

(i) The FDA has received an abbreviated new drug application from Cheminor containing bioavailability or bioequivalence data or information with respect to fluoxetine hydrochloride 10 and 20 mg capsules.

(ii) The abbreviated new drug application number is 75-465.

(iii) The letter refers to the proposed drug product as fluoxetine capsules, 10 and 20 mg. (The established name, as defined in Section 502(e)(3) of the Food, Drug and Cosmetic Act, of the proposed drug product is fluoxetine hydrochloride capsules 10 and 20 mg.)

(iv) The active ingredient, strength, and dosage form of the proposed drug product is fluoxetine hydrochloride 10 and 20 mg capsules for oral administration.

(v) The patent numbers and expiration dates, as known to Cheminor, each claim of which is alleged to be either invalid or not infringed, is as follows:

United States Patent No. 4,626,549, which expires December 2, 2003.

(2) Lilly received the letter on or about November 30, 1998.

Certification

We hereby certify that on January 11, 1999, Lilly filed an action for patent infringement against Cheminor in the United States District Court for the Southern District of Indiana (Case Number IP99-0024 C B/S). Lilly alleges, among other things, that under 35 U.S.C. § 271(e)(2)(A), Cheminor's submission to the FDA of an abbreviated new drug application to obtain approval for the commercial manufacture, use, or sale of fluoxetine hydrochloride before the expiration of United States Patent No. 4,626,549 was an act that infringes claims 6 and 7 of United States Patent No. 4,626,549.

We therefore respectfully request that the approval of Cheminor's abbreviated new drug application shall not be made effective until at least the expiration of the thirty-month period as provided by 21 U.S.C. § 355(j)(4)(B)(iii), subject to an appropriate ruling by the Court.

Yours sincerely,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

By David S. Forman
David S. Forman

DSF/mco/mrm

cc: Cameron Reid, President
Reddy-Cheminor, Inc.

REDDY-CHEMINOR, INC. Rx-C

66 South Maple Avenue
Ridgewood, New Jersey 07450
Telephone (201) 444-4424
Telefax (201) 444-1456

January 20, 1999

NEW CORRESP
NC

Mr. Tim Ames, Project Manager
Regulatory Support Branch
FDA-Office of Generic Drugs
MPN II, HFD-615
7500 Standish Place, Room 150
Rockville, MD 20855

RE: PATENT AMENDMENT/DOCUMENTATION OF LITIGATION
Cheminor Drugs Ltd./ANDA 75-465
Fluoxetine Capsules USP, 10 mg and 20 mg

Dear Mr. Ames:

As provided for in section 505 (j) (4) (B) (iii) of the Act, Reddy-Cheminor Inc., authorized to act on behalf of Cheminor Drugs Ltd., hereby advises the Agency of receipt of Complaint for Patent Infringement.

As required, we hereby provide a copy of Complaint for Patent Infringement filed in the US District Court, Southern District of Indiana listing Eli Lilly and Company (Plaintiff) v. Cheminor Drugs Ltd. and Reddy-Cheminor, Inc. (Defendant). Further attached, please find Form FDA 356h.

Please do not hesitate to contact us should you have any questions or require additional information.

With best regards,

REDDY-CHEMINOR, INC.

Paul V. Campanelli
Vice President, Formulations Business

RECEIVED
JAN 21 1999

Attachments

REDDY-CHEMINOR, INC.

66 South Maple Avenue
Ridgewood, New Jersey 07450
Telephone (201) 444-4424
Telefax (201) 444-1456

December 10, 1999

ORIG AMENDMENT

N/AA

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Amendment

Reference : Fluoxetine Capsules, USP, 10 mg, 20 mg and 40 mg
ANDA 75-465

Dear Sir/ Madam:

Please refer to pending ANDA 75-465 for Fluoxetine Capsules, USP, 10 mg and 20 mg, submitted on September 24, 1998 and to the amendment dated September 20, 1999, providing for the additional dosage strength of Fluoxetine Capsules, USP, 40 mg. Reddy-Cheminor, Inc., U.S. agent for Cheminor Drugs Limited (CDL), herewith submits an amendment to the above referenced abbreviated new drug application providing for additional information regarding Fluoxetine Capsules, USP, 40 mg.

In Section XVII of the September 20, 1999 amendment, CDL indicated that controlled room temperature (CRT) (25°C ± 2°C and 60% ± 5% relative humidity) and accelerated (40°C ± 2°C and 75% ± 5% relative humidity) stability studies for Fluoxetine Capsules, USP, 40 mg, Lot E001 were ongoing. The stability study results have become available at this time, and CDL is amending ANDA 75-465 to include the Stability Protocol, Expiration Dating Period, Stability Data and Stability Summary (Exhibit I).

CDL has three intended commercial packaging configurations for Fluoxetine Capsules, USP, 40 mg: 30 fill/60 cc/33 mm closure, 100 fill/150 cc/38 mm closure and 500 fill/750cc/53 mm closure. In the September 20, 1999 amendment, CDL provided container/closure test data for only the smallest and largest container/closure sizes. At this time CDL is amending the ANDA to also include container/closure testing for the 100 fill/150 cc/38 mm closure packaging configuration. Exhibit II contains the test data for the High Density Polyethylene Containers (150 cc) which should be included following page 706 in Section XIV of the September 20, 1999 amendment. In addition, Exhibit III contains the test data for the Child Resistant Plastic caps with Pulp Liners (38 mm) which should be included following page 734 in Section XIV of the September 20, 1999 amendment.

Pursuant to 21 CFR § 314.440 (a) (4), a third copy of this application is also enclosed. This is the required field copy and we certify that it is a true copy of the technical section as described in 21 CFR § 314.50 (d) (1).

Included in this submission is an extra copy of our cover letter. Please acknowledge by date stamping this letter upon receipt and forwarding this copy to us in the self-addressed stamped envelope provided for your convenience.

Please contact the undersigned at (201) 444-4424 or by fax at (201) 444-1456 you have any questions concerning this submission.

Sincerely,

Paul V. Campanelli
Vice President
Formulations Business
Reddy-Cheminor, Inc.

REDDY-CHEMINOR, INC. Rx-C

66 South Maple Avenue,
Ridgewood, NJ 07450
Phone: 201-444-4424
Fax: 201-444-1456

labeling reviewed drafted 6/7/01 A. Vezza

HAND DELIVERED

May 25, 2001

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ORIG AMENDMENT

Judy Nemes NTI 5/30/01

AT of Patent Info

Reference: **ANDA 75-465 Fluoxetine Capsules USP, 10 mg, 20 and 40 mg**
Labeling Amendment

Dear Sir/ Madam:

Reddy-Cheminor Inc., US Agent for Dr. Reddy's Laboratories Limited, here within submits a response to the Labeling Deficiency Letter dated April 6, 2001 (referencing both ANDA 76-006 and ANDA 75-465) pursuant to Section 505 (j) of the Federal Food, Drug, and Cosmetic Act. Reference is also made to the Agency's letter dated March 16, 2001.

The Firm is submitting an amended patent certification, a summary of changes, and final printed copies of the proposed outsert and labels. The Firm has deleted the references to tablets in the "Description" and "How supplied" sections. At this time, the Firm believes that it will market the 40 mg capsule in advance of the other strengths. For that reason the HOW SUPPLIED section contains only a reference for the 40 mg capsule. References to blisters are also deleted at this time. Prior to marketing the other strengths, and packaging, the Firm will submit an amendment/supplement to provide the other strengths, as per Adolf Vezza. Also, the A-A code on the label copy for the 40 mg capsules, adjacent to the bar code, will not appear on the market labels.

ANDA 75-465 Fluoxetine Capsules USP, 10 mg, 20 and 40 mg
Labeling Amendment

Labeling Deficiencies:

1. *GENERAL COMMENTS*

   a. *Please note that you may not leave all bulimia information out of the package insert labeling without doing a Paragraph IV certification and making a method of use statement (section viii) to patent ('549). We refer you to the Agency's letter dated March 16, 2001 for guidance.*

      There were no references to bulimia in the last submission.

      As requested the Paragraph IV certification is amended and a method of use statement (section viii) to U.S. Patent 4,626,549 is provided in compliance with the agency letter, dated March 16, 2001.

   b. *Because this application shares an insert with ANDA 75-465 (capsules) both must be approved together or further insert labeling revisions would be necessary.*

      The insert for ANDA 75-465 (capsules) no longer references the tablets and has been submitted under separate cover to that application.

2. *INSERT*

   The Firm made all of the necessary changes listed below. Some of the requested changes did not apply to our last submission and are noted below.

   a. *GENERAL COMMENT*

      Replace " with "TCA"
      and "TCAs" respectively except where indicated below.

   b. *CLINICAL PHARMACOLOGY*

   i. *Pharmacodynamics, second paragraph – "...tricyclic antidepressant (TCA) drugs."*

   ii. *Absorption, Distribution, Metabolism, and Excretion*

      A. *Systemic Bioavailability, second paragraph, first sentence – "The capsule, tablet and oral solution dosage forms of Fluoxetine..."*

      B. *Metabolism, first sentence – "...other unidentified..." (delete comma)*

      C. *Accumulation and Slow Elimination, first paragraph, last sentence –*

         a. *"Steady-state..." (add hyphen)*

         b. *"...at 4 to 5 weeks." ("to" rather than "-")*

iii. Clinical Trials, Depression, second paragraph, first sentence

A. "(N=671, randomized)" (add comma)

B. "...fluoxetine 20 mg..." (delete comma – two instances)

b. PRECAUTIONS

i. General

A. Anxiety and insomnia, second paragraph, first sentence – "OCD" rather than "obsessive compulsive disorder"

B. Suicide, first paragraph, last sentence – Delete

a. Delete

There were no references to bulimia in this submission.

b. Delete

There were not references to bulimia in this submission.

ii. Drug Interactions

A. Drugs Metabolized by P450IIIA4, fist sentence – "coadministration" (delete hyphen)

B. Other Antidepressants, third sentence – "...dose of TCA may need..."

C. Warfarin – "anticoagulant" and "coadministered" (delete hyphens)

iii. Carcinogenesis, Mutagenesis, Impairment of Fertility –" ... mutagenicity, or..."(add comma)

iv. Pregnancy—Pregnancy Category C, first sentence – "...basis), throughout..." (add comma)

v. Geriatric Use, third sentence – "...patients, see..." (add comma)

c. ADVERSE REACTIONS

Associated with Discontinuation in U.S. – "only" rather than

d. OVERDOSAGE

i. *Animal Experience, second paragraph –"...mg/kg, respectively." (add comma)*

ii. *Management of Overdose, last paragraph, last sentence – "for" rather than*

e. *DOSAGE AND ADMINISTRATION*

i. *Depression, Initial Treatment, fourth paragraph, last sentence – "...(see Liver Disease and Renal..." (italic "and")*

A. *Maintenance/Continuation/Extended Treatment – The sentence beginning "Systematic evaluation..." begins a new paragraph.*

This change was already made in the prior submission.

ii. *Switching Patients to a Tricyclic Antidepressant (TCA) – "... under PRECAUTIONS, Drug Interactions)."*

f. *HOW SUPPLIED*

i. *Add an asterisk after each strength in the established names and add the following statement:*
"fluoxetine base equivalent (present as the hydrochloride)

ii. *Add the statement "PROTECT FROM LIGHT."*

g. *ANIMAL TOXICOLOGY*

Last sentence – "in" rather than

All of the above listed changes have been made. In addition, the Firm corrected two typographical errors on the spelling of the words *treatment* and *compulsive*. Additionally, in several sections, the spacing after "– " has been corrected to be consistent throughout the outsert. The "(see USP)" was changed to "(see USP)". These changes are listed in Section 5 Comparison and provided in Section 6 Labeling.

This concludes our response to the labeling deficiency letter. Please contact C. Jeanne Taborsky, at tele. (410) 309-3145, FAX (410) 309-6145, or Paul V. Campanelli, Vice President Formulations-Business, Reddy-Cheminor, Inc. at (201) 444-4424 or by fax at (201) 444-1456, if you have any questions concerning this submission.

Sincerely yours,

C. Jeanne Taborsky

C. Jeanne Taborsky
Regulatory Affairs Consultant

REDDY-CHEMINOR, INC.

66 South Maple Avenue
Ridgewood, New Jersey 07450
Telephone (201) 444-4424
Telefax (201) 444-1456

MARCH 30, 2001

Via Facsimile – 4 pages (301) 443-3839 and Courier

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ORIG AMEND

FA

Telephone Amendment

Reference: **Fluoxetine Capsules, USP 10 mg, 20 mg and 40 mg**
ANDA 75-465

Dear Sir/ Madam:

This is in reference to your Telephonic conversation dated March 29, 2001 regarding our pending ANDA # 75-465 for Fluoxetine Capsules, USP 10 mg, 20 mg and 40 mg. Reddy – Cheminor, Inc., US Agent for Dr. Reddy's Laboratories Limited herewith submits Telephone Amendment to the above referenced ANDA to include the following information in response to the Agency's Comments:

FDA Comment:

1. **In the specifications of Fluoxetine Hydrochloride, USP active raw material, the limits of residual solvents. Acetonitrile should be tightened from NMT ppm to NMT ppm (ICH limit) and should be tightened from NMT ppm to NMT ppm (ICH limit).**

Response

In response to the Agency's comment, the limit of Acetonitrile has been tightened to NMT ppm and the limit of is tightened to NMT ppm, in line with the ICH requirements. The revised specifications of Fluoxetine Hydrochloride, USP is provided in ***Exhibit – I.***

Please contact the undersigned at (201) 444-4424 or by fax at (201) 444-1456, if you have any questions concerning this submission.

Sincerely,

CENTER FOR DRUG EVALUATION AND RESEARCH
APR 04 2001
OGD

Paul V. Campanelli
Vice President, Formulations Business
Reddy-Cheminor, Inc.
(US Agent for Dr. Reddy's Laboratories Limited)

7.1

ANDA 76-006
75-465

MAR 16 2001

Reddy-Cheminor, Inc.
U.S. Agent for Dr. Reddy's Laboratories Limited
Attention: Paul V. Campanelli
66 South Maple Avenue
Ridgewood, NJ 07450

Dear Sir:

The Office of Generic Drugs (OGD) has reconsidered its position regarding the applicability of a listed patent to portions of the labeling of the reference listed drug, Prozac®, (fluoxetine hydrochloride) NDA 18-936, NDA 20-101 and NDA 20-974. This relates to U.S. patent number 4,626,549, which is listed in the Orange Book as covering two uses of fluoxetine hydrochloride. Use 84 is described by the NDA holder as " a method of blocking the uptake of monoamines by brain neurons in animals." Use 154 is described as "a method of treating animals suffering from an appetite disorder." Specifically, the Agency has concluded that applicants may remove statements related to "appetite disorders" from the proposed ANDA labeling. The Agency permits firms to omit from the labeling indications that are protected by patent and/or exclusivity pursuant to Section 505(j)(2)(A)(viii) of the Federal Food Drug and Cosmetic Act and 21 C.F.R. § 314.94(a)(8)(iv).

The labeling of the reference listed drug, Prozac®, includes the following indication: "*Bulimia Nervosa* --Prozac® is indicated for the treatment of binge-eating and vomiting behaviors in patients with moderate to severe bulimia nervosa." We find that it is reasonable to consider bulimia an appetite disorder. One of the definitions in Dorland's Illustrated Medical Dictionary, 28th Edition, characterizes bulimia as an "abnormally increased appetite; hyperorexia".

Therefore, ANDA applicants may omit the statements related to "appetite disorders" from the labeling of their generic version of fluoxetine hydrochloride. The applicants are permitted to amend their paragraph IV (PIV) patent certification to the '549 patent to assert that the labeling does not infringe the patent or that the patent is invalid or unenforceable for some of the claims and also include a statement under Section 505(j)(2)(A)(viii) and 21 CFR § 314.94(a)(12)(iii) (a "section viii statement") that indicates that the method of use patent does not claim a use for which the ANDA applicants are seeking approval for other claims. In this case, because the '549 patent apparently contains a number of different claims described by the NDA holder as covering different uses, the section viii statement will essentially assert that the ANDA applicants are not seeking approval for one or more of the multiple uses claimed in the patent. In addition, the ANDA applicants are requested to specify the use(s) they are deleting from the labeling.

If you have any questions regarding this correspondence, please contact Cecelia Parise, R.Ph., Special Assistant for Regulatory Policy, Office of Generic Drugs, at (301) 827-5845.

Sincerely,

Robert L. West for
3/16/2001

Gary Buehler
Acting Director
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 76-006; 75-465
Liz Dickinson, GCF-1
Kim Dettelbach, GCF-1
Adolph Vezza, HFD-613
Charlie Hoppes, HFD-613
Peter Rickman, HFD-610
Greg Davis, HFD-615
Don Hare, HFD-600
Rita Hassall, HFD-600
Cecelia Paris, HFD-600
Robert West, HFD-600
Gary Buehler, HFD-600

Drafted by: C. Parise 3/8/01
Revised by: L. Dickinson 3/13/01
Revised by: C. Parise 3/14/01
Edited by: P. Downs 3/14/01
Revised by: G. Buehler 3/14/01

REDDY-CHEMINOR, INC.

66 South Maple Avenue
Ridgewood, New Jersey 07450
Telephone (201) 444-4424
Telefax (201) 444-1456

March 8, 2001

N|FA

ORIG AMENDMENT

UPS NEXT DAY AIR: 1ZE067822210012369
Via Facsimile: 301 443-3839
4 pages

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773
Attention: Bonnie McNeal

Telephone Amendment

Reference: Fluoxetine Capsules, USP, 10 mg, 20 mg and 40 mg, ANDA # 75-465.

Dear Ms. McNeal:

This is in reference to your letter dated March 8, 2001; regarding our pending ANDA 75-465 for Fluoxetine Capsules, 10 mg, 20 mg and 40 mg submitted on September 24, 1998. We would like to confirm that the Agency inadvertently issued the attached deficiency letter dated March 8, 2001 with respect to an outstanding labeling deficiency response.

Per our teleconference with you, the Agency has confirmed receipt of our labeling deficiency on February 6th. Further, attached, please find a copy of a USP Tracking Summary confirming delivery on February 6th.

Please contact the undersigned at (201) 444-4424 or by fax at (201) 444-1456 if you have any questions regarding this submission.

Very truly yours,

REDDY-CHEMINOR, INC.

CENTER FOR DRUG EVALUATION AND RESEARCH
RECD
MAR 0 9 2001
OGD

Paul V. Campanelli
Vice President, Formulations Business

Attachments

REDDY-CHEMINOR, INC. Rx-C

66 South Maple Avenue,
Ridgewood, NJ 07450

Phone: 201-444-4424
Fax: 201-444-1456

NC

VIA FED X

February 07, 2001

NEW CORRESP

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Reference: 75-465 Fluoxetine Capsules USP, 10, 20, and 40 mg
Correspondence

This correspondence is being provided by the US Agent on behalf of Cheminor Drugs Limited (Pharma Division), Via IDA Bollaram, Bachepalli - 502 325, INDIA. On January 2, 2001, the Andhra Pradesh High Court ruled on the merger of Cheminor Drugs Limited and Dr. Reddy's Laboratories. As of that date, Cheminor Drugs Limited is known as Dr. Reddy's Laboratories Limited.

The address and all other information remain the same. Documents have been filed to change the Registration Number and labeler code to that of Dr. Reddy's Laboratories Limited.

Pursuant to *Code of Federal Regulations* Title 21 § 314.440 (a) (4), a Field Copy of this correspondence is being submitted to the Office of Generic Drugs. The Firm hereby certifies that it is a true copy of the technical section as described in 21 CFR 314.50 (d) (1).

Thank you for your assistance in this matter. Please feel free to contact us if necessary.

Sincerely yours,

C. Jeanne Taborsky
Regulatory Affairs Consultant

CENTER FOR DRUG EVALUATION AND RESEARCH
RECD
FEB - 8 2001
OGD

2-14-01

REDDY-CHEMINOR, INC. Rx-C

66 South Maple Avenue
Ridgewood, New Jersey 07450
Telephone (201) 444-4424
Telefax (201) 444-1456

NAI
12/13/99 NEW CORRESP
NC

November 18, 1999

Patent / Suit info recorded!
12/13/99

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773
Attention: Lieutenant Greg Davis

Patent Amendment

Reference: Fluoxetine Capsules, USP, 10 mg, 20 mg and 40 mg
ANDA 75-465

Dear Sir or Madam:

Under the provisions of 21 CFR § 314.95(e), Reddy-Cheminor, Inc., a subsidiary of Cheminor Drugs Ltd., is amending our pending ANDA 75-465 for Fluoxetine Capsules, USP, 10 mg, 20 mg and 40 mg, submitted on September 20, 1999, to provide for additional patent certification information.

Reddy-Cheminor hereby certifies it has complied with the requirements of 21 CFR § 314.95(a) & (b) by sending a Notice of Certification to Eli Lilly and Company, the owner of U.S. Patent No. 4,626,549 and holder of approved application NDA 18-936 for Prozac® (fluoxetine hydrochloride) capsules 10 mg, 20 mg and 40 mg and that Notice met the content requirement under 21 CFR § 314.95(c).

A Notice of Certification was sent to Eli Lilly and Company in Indianapolis, Indiana via U.S. Postal Certified Return Receipt. The return receipt shows that Eli Lilly received the Notice on September 28, 1999 (Exhibit 1).

On November 3, 1999, Schein Pharmaceutical, Inc., Cheminor Drugs Ltd., and Reddy-Cheminor, Inc. were served with a Complaint filed in the United States District Court for the Southern District of Indiana, Civil Action IP99-1697 C-B/S (Exhibit 2) by Eli Lilly and Company in response to Cheminor's ANDA for Fluoxetine Capsules, USP, 10 mg, 20 mg and 40 mg.

Further, we would like to advise the FDA that this is a second complaint served to Cheminor and Reddy-Cheminor. Lilly's initial complaint was filed on

January 11, 1999 (Exhibit 3) with respect to Fluoxetine Capsules, USP, 10 mg and 20 mg.

Included in this submission is an extra copy of our cover letter. Please acknowledge by date stamping this letter upon receipt and forwarding this copy to us in the self-addressed stamped envelope provided for your convenience.

Please contact the undersigned at 201-444-4424 or by fax at 201-444-1456 if you have any questions regarding this submission.

Sincerely,

REDDY-CHEMINOR, INC.

Paul V. Campanelli
Vice President, Formulations Business

Cheminor Drugs Limited

Pharma Division

labeling review drafted 11/15/99 A. Vezza

September 20, 1999

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

VIA U.S. AMENDMENT
AA

Reference : **Major Amendment to Abbreviated New Drug Application Fluoxetine Capsules, USP, 10 mg and 20 mg # 75-465 to include Fluoxetine Capsules, USP, 40 mg as additional dosage strength**

Dear Sir/ Madam:

Cheminor Drugs Limited herewith submits an amendment to the above referenced abbreviated new drug application, to include Fluoxetine Capsules, USP, 40 mg as additional dosage strength.

This ANDA amendment refers to the listed drug, PROZAC® (Fluoxetine Hydrochloride) Capsules, 40 mg which is manufactured by ELI LILLY and Co. who is the holder of the approved application. U.S. Patent No. 4314081 will expire on Feb 02, 2001. Cheminor Drugs Limited is not seeking to market the product until after the patent expires. Cheminor Drugs Limited certifies that U.S. Patent No. 4626549 (expiration date Dec 02, 2003) is invalid, unenforceable, or will not be infringed by the manufacture, use or sale of Fluoxetine Capsules, USP, 40 mg for which this amendment is submitted. The exclusivity for indication for the treatment of bulimia expires on Nov 21, 1999. Cheminor Drugs Limited will not market the product with the indication noted above until after the market exclusivity expires.

Fluoxetine Hydrochloride Capsules, USP, 40 mg have been developed at Cheminor Drugs Limited, Via IDA Bollaram, Bachepalli - 502 325, INDIA in accordance with 21 CFR 210 and 211.

The manufacturer of the drug substance used to produce the ANDA batch of this product is : Dr.Reddy's Laboratories, Hyderabad, INDIA, DMF No.

The required bioavailability / bioequivalence studies were conducted on Fluoxetine Capsules, USP, 20 mg and PROZAC® (Fluoxetine Hydrochloride) Capsules, 20 mg by

These studies indicate that Fluoxetine Capsules, USP, 20 mg, is bioequivalent to PROZAC® (Fluoxetine Hydrochloride) Capsules, 20 mg.

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
SEP 20 1999
OGD

Cheminor Drugs Limited

Pharma Division

September 20, 1999

Food and Drug Administration
Fluoxetine Capsules, USP, 40 mg
Abbreviated New Drug Application # 75-465

The bioequivalence / bioavailability study report for Fluoxetine Capsules, USP, 20 mg is already submitted in our original ANDA # 75-465. The total dose administered to subjects in both these studies was 40 mg (2 x 20 mg capsules).

The 40 mg formulation is dose proportional to our Fluoxetine Capsules, USP, 20 mg formulation, therefore a waiver of in-vivo bioavailability / bioequivalence study requirements for Fluoxetine Capsules, USP, 40 mg is requested.

The in-vitro dissolution profile for Fluoxetine Capsules, USP, 40 is comparable to PROZAC® (Fluoxetine Hydrochloride) Capsules, 40 mg.

The dosage form, route of administration, active ingredient, potency and labeling (except Description, How Supplied and text covered by patents/exclusivities) for Fluoxetine Capsules, USP, 40 mg is the same as PROZAC® (Fluoxetine Hydrochloride) Capsules, 40 mg.

This ANDA amendment is submitted in two volumes:

Schein Pharmaceutical, Inc. will be the distributor for these products. The proposed labeling has been prepared using the Schein Pharmaceutical logo, etc. Following this letter is a letter authorizing Reddy-Cheminor, Inc. to act as the U.S. agent for this ANDA. Included in this submission is an extra copy of our cover letter. Please acknowledge by date stamping this letter upon receipt and forwarding this copy to us in the self addressed stamped envelope provided for your convenience.

Cheminor Drugs Limited

Pharma Division

Date September 20, 1999

Food and Drug Administration
Fluoxetine Capsules, USP, 40 mg
Abbreviated New Drug Application # 75-465

Pursuant to 21CFR 314.440 (a) (4), a third copy of this application is also enclosed. This is the required field copy and we certify that it is a true copy of the technical section as described in 21 CFR 314.50 (d) (1).

Sincerely,

R.S. Prasad
Senior Vice President

labeling review drafted 1/10/01 AV

REDDY-CHEMINOR, INC.

66 South Maple Avenue
Ridgewood, New Jersey 07450
Telephone (201) 444-4424
Telefax (201) 444-1456

December 26, 2000

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

NDA ORIG AMENDMENT
N/FA

Fax Amendment

Reference: Fluoxetine Capsules, USP, 10 mg, 20 mg and 40 mg, ANDA # 75-465.

Dear Sir/ Madam:

This is in reference to your letter dated Nov 16, 2000 regarding our pending ANDA 75-465 for Fluoxetine Capsules, 10 mg, 20 mg and 40 mg submitted on September 24, 1998. Cheminor Drugs Limited (CDL) herewith submits the following **"Fax Amendment"** that includes information in response to the Agency's Correspondence:

Chemistry Comments:

FDA Comment

1. **The proposed specification of 100 ppm for residual in the drug substance (Fluoxetine Hydrochloride) and Pregelatinized Starch NF release specifications is too high. Although the USP 24/NF 19 OVI test does not include a limit for for all compendial articles, the current office policy still requires assurance that is either absent or present at levels NMT 2 ppm in pharmaceutical components. Please tighten the limit for to 2 ppm. Alternatively, you may submit certification from the manufacturers of the pharmaceutical components for absence of**

Response:

As per agency's recommendation, the limits for OVI have been revised to 2 ppm in the specifications of Fluoxetine Hydrochloride, USP and Pregelatinized Starch, NF. The revised specifications are provided in *Exhibit – I.*

Please also note that, we have already submitted the declaration from the supplier of the active raw material (Fluoxetine HCl) stating that "No USP specified Organic Volatile Impurities have been used in the manufacturing process". (Please see page # 281 of our ANDA Amendment dated Sept. 20th, 1999).

Labeling Comments:

FDA Comment

1. CONTAINER 30s and 100s (10 mg, 20 mg and 40 mg) – 500s (40 mg) – 1000s (20 mg).

   Please note that for computer-generated labels to be acceptable as final print, they must be of actual size, color and clarity. Please assure that these criteria are met prior to submission of final print.

Response:

We acknowledge the Agencies Comment that final labels are required for final approval. We request the agency to grant the tentative approval based on the draft labeling.

FDA Comment

2. INSERT

   We acknowledge your amendment dated May 9, 2000. We note that you are not claiming the indication, Obsessive Compulsive Disorder (OCD), and that you have deleted reference to that indication in your insert labeling.

   The regulations for generic drug labeling, 21 CFR 314.94(a)(8)(iv), state in relevant part, that labeling proposed by the applicant, ".... must be the same as the labeling approved for the reference listed drug except for .... omission of an indication or other aspect of labeling protected by patent or accorded exclusivity..." Unless there is a patent or exclusivity that covers OCD, you must retain that indication in your labeling.

   Our office does not have expertise in the interpretation of patents. Since no patent listed in the Orange Book specifically claims OCD, we ask that you request clarification as to whether that indication is the subject of any patent.

   We acknowledge your Paragraph IV certification to patent 4,626,549 and we believe there should be clarification regarding this patent, and that it should be specifically associated (or not associated) with the indications appearing in the labeling for the reference listed drug.

   To clarify whether OCD is specifically claimed by a patent, we refer you to 21 CFR 314.53(f) "Correction of patent information errors". Please follow the procedure outlined by that regulation to request clarification through HFD-90, Division of Data Management.

   Please copy your application to HFD-90. Please also provide a desk copy to Adolph Vezza.

Response:

The obsessive compulsive Disorder is included in the insert and explained in the Side-by-Side Comparison between the previously submitted insert issued May, 2000 and our proposed insert December, 2000.

We confirm that, the Paragraph IV Certification to patent 4,626,549 is not associated with any indications appearing in the labeling. The revised insert and side-by-side comparison are provided in Exhibit – II.

Please contact the undersigned at (201) 444-4424 or by fax at (201) 444-1456 if you have any questions regarding this submission.

Sincerely,

Paul V. Campanelli
Vice President
Formulations Business
Reddy-Cheminor, Inc.

REDDY-CHEMINOR, INC.

66 South Maple Avenue
Ridgewood, New Jersey 07450
Telephone (201) 444-4424
Telefax (201) 444-1456

September 26, 2000

NDA ORIG AMENDMENT
AB

Office of Generic Drugs
Food and Drug Administration
Center for Evaluation and Research
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Bioequivalency Amendment

Reference: Fluoxetine Hydrochloride Capsules, USP, 10 mg, 20 mg and 40 mg
ANDA 75-465

Dear Sir/Madam:

This is in reference to your letter dated May 17, 2000 regarding pending ANDA 75-465 for Fluoxetine Hydrochloride Capsules, USP, 10 mg, 20 mg and 40 mg, submitted September 24, 1998. Reddy-Cheminor, Inc., U.S. Agent for Cheminor Drugs Limited (CDL), is providing the following information in response to the Bioequivalency Deficiencies stated in the May 17, 2000 letter.

As requested CDL has conducted a fasting bioequivalence study on our Fluoxetine Hydrochloride Capsules, USP, 40 mg product. This study demonstrates that CDL's Fluoxetine Hydrochloride Capsules, USP, 40 mg are bioequivalent to Prozac® Capsules, 40 mg.

Dissolution studies comparing CDL's Fluoxetine Hydrochloride Capsules, USP, 40 mg (Lot E001) with the referenced listed drug, Prozac® Capsules, 40 mg (Lot 2ND49M) are included in Exhibit I. The dissolution method used in generating the profile data is located on pages 257-260, Section VI of the September 20, 1999 amendment to ANDA 75-465. Copies of the certificates of analysis for the respective drug product lots are provided in Exhibit II.

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
SEP 27 2000
OGD

The required bioavailability/bioequivalence study was conducted by

. Certification: Financial Interests and Arrangements of Clinical Investigators, is located in Exhibit III.

The full report for bioequivalence Protocol No. 000632 "Comparative, Randomized, Single-Dose, 2-Way Crossover Bioequivalence Study of CDL's Fluoxetine Hydrochloride Capsules, USP, 40 mg and Eli Lilly and Company's Prozac® Capsules, 40 mg in Healthy Adult Males Under Fasting Conditions" is provided in Exhibit IV.

Included in this submission is an extra copy of our cover letter. Please acknowledge by date stamping this letter upon receipt and forwarding this copy to us in the self-addressed stamped envelope provided for your convenience.

Please contact the undersigned at (201) 444-4424 or by fax at (201) 444-1456 if you have any questions concerning this submission.

Sincerely,

Paul V. Campanelli
Vice President
Formulations Business
Reddy-Cheminor, Inc.

U.S. Agent for Cheminor Drugs Limited

cc: Jennifer Fan, Project Manager, Division of Bioequivalence, OGD (fax copy)