CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number: NDA 20639

Trade Name: SEROQUEL

Generic Name: QUETIAPINE FUMARATE

Sponsor: ZENECA PHARMACEUTICALS

Approval Date: SEPTEMBER 26, 1997

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION: NDA 20639

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Chemistry Review(s)	X			
EA/FONSI	X			
Pharmacology Review(s)	X			
Statistical Review(s)	X			
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Application Number: NDA 20639

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-639

SEP 26 1997

Zeneca Pharmaceuticals
Attention: W.J. Kennedy, Ph.D.
1800 Concord Pike
PO Box 15437
Wilmington, DE 19850-5437

Dear Dr. Kennedy:

Please refer to your new drug application dated and received July 29, 1996, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Seroquel (quetiapine fumarate) 25, 100, and 200 mg tablets.

We acknowledge receipt of your submissions of July 31, 1997, August 6, 1997, and August 7, 1997. The original User Fee goal date for this application was July 29, 1997. Your submission of July 31, 1997, extended the User Fee goal date to February 4, 1998.

This new drug application provides for a new chemical entity indicated for the treatment of the manifestations of psychotic disorders.

We have completed the review of this application, including the submitted draft labeling, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the enclosed marked-up draft labeling. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed marked-up draft labeling. Marketing the product with FPL that is not identical to this draft labeling may render the product misbranded and an unapproved new drug.

The enclosed labeling is identical to the labeling mutually agreed to in (1) an August 21, 1997, teleconference with agency staff that addressed all labeling issues except language in the "Cataracts" subsection under Precautions, General, and (2) an August 28, 1997 meeting with agency staff during which agreement was reached on labeling language for the cataract statement.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FINAL PRINTED LABELING" for approved NDA 20-639. Approval of this submission by FDA is not required before the labeling is used.

Should additional information relating to the safety and effectiveness of the drug become available, revision of that labeling may be required.

We remind you of the following Phase 4 commitments, specified in your submission of July 31, 1997, and further discussed in the meeting of August 28, 1997:

Protocols, data, and final reports should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. Should an IND not be required to meet your Phase 4 commitments, please submit protocol, data, and final reports to this NDA as correspondences. In addition, we request under 21 CFR 314.81(b)(2)(vii) that you include in your annual report to this application, a status summary of each commitment. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements, relating to these Phase 4 commitments must be clearly designated "Phase 4 Commitments."

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact Steven D. Hardeman, R.Ph., Project Manager, at (301) 594-5533.

Sincerely yours,

Robert Temple 9/26/97

Robert Temple, M.D.
Director
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Attachment (labeling)

APPEARS THIS WAY
ON ORIGINAL

APPEARS THIS WAY
(illegible)

APPEARS THIS WAY
(illegible)

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APPLICATION NUMBER: NDA 20639

APPROVABLE LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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NDA 20-639

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Dear Dr. Kennedy:

Please refer to your new drug application dated and received July 29, 1996, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Seroquel (quetiapine fumarate) 25, 100, and 200 mg tablets.

We acknowledge receipt of the following submissions:

July 29, 1996	August 14, 1996	September 5, 1996	September 9, 1996
September 20, 1996	September 30, 1996	October 3, 1996	October 14, 1996
October, 16, 1996	October 28, 1996	November 27, 1996	December 27, 1996
January 7, 1997	January 16, 1997	January 21, 1997	February 3, 1997
February 17, 1997	February 21, 1997	February 25, 1997	February 27, 1997
March 6, 1997	March 26, 1997	March 27, 1997	April 14, 1997
April 29, 1997	May 5, 1997	June 16, 1997	June 19, 1997
June 23, 1997	June 26, 1997	June 30, 1997	

The User Fee goal date for this application is July 29, 1997.

We have completed the review of this application as submitted with draft labeling, and it is approvable. Before this application may be approved, however, it will be necessary for you to respond to the following requests:

1. **Labeling**

Accompanying this letter (Attachment 1) is the Agency's proposal for the labeling of Seroquel. We believe it presents a fair summary of the information available on the benefits and risks of Seroquel.

We have proposed a number of changes to the draft labeling submitted in your original submission. We will be happy to discuss these proposed changes in detail, and to discuss any disagreements you might have with any part of the proposed labeling format or content.

2. Post-marketing Studies

3. Safety Update

Our assessment of the safety of Seroquel is based on our review of all safety information provided in your original and subsequent submissions, including your safety update of November 27, 1996. This original review was based on an integrated safety database and serious adverse event reporting with a cutoff date of approximately March 1, 1996. Under 21 CFR 314.50(d)(5)(vi)(*b*), we request that you provide a final safety update focusing on deaths, serious adverse events, and dropouts for adverse events.

4. World Literature Update

Prior to the approval of Seroquel, we require an updated report on the world's archival literature pertaining to the safety of Seroquel. This report should include only literature not covered in your previous submissions. We need your warrant that you have reviewed this literature systematically, and in detail, and that you have discovered no finding that would adversely affect conclusions about the safety of Seroquel. The report should also detail how the literature search was conducted, by whom (their credentials) and whether it relied on abstracts or full texts (including translations) of articles. The report should emphasize clinical data, but new findings in preclinical reports of potential significance should also be described. Should any report or finding be judged important, a copy (translated as required) should be submitted for our review.

5. Foreign Regulatory Update/Labeling

We require a review of the status of all Seroquel actions taken or pending before foreign regulatory authorities. Approval actions can be noted, but we ask that you describe in detail any and all actions taken that have been negative, supplying a full explanation of the views of all parties and the resolution of the matter. If Seroquel is approved by any non-US regulatory bodies, we ask that you provide us any approved labeling for Seroquel along with English translations when needed.

6. Biopharmaceutics

Please adopt the following dissolution methodology and specification for all tablet strengths:

Apparatus:
Speed:
Medium:
Specification:

In addition, it will be necessary for you to submit final printed labeling (FPL) identical in content to the enclosed marked-up draft labeling. Please submit 20 copies of the final printed labeling, ten of which are individually mounted on heavy-weight paper or similar material.

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

In addition, please submit three copies of the introductory promotional material that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional material and the package insert directly to:

Food and Drug Administration
Division of Drug Marketing, Advertising
and Communications, HFD-40
5600 Fishers Lane
Rockville, Maryland 20857

Within 10 days after the date of this letter, you are required to amend the application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of such action FDA may take action to withdraw the application.

Under 21 CFR 314.102(d) of the new drug regulations, you may request an informal meeting or telephone conference with the Division to discuss what further steps need to be taken before the application may be approved.

The drug may not be legally marketed until you have been notified in writing that the application is approved.

If you have any questions, please contact Steven D. Hardeman, R.Ph., Project Manager, at (301) 594-5533.

Sincerely yours,

Robert Temple, M.D.
Director
Office of Drug Evaluation I
Center for Drug Evaluation and Research

APPEARS THIS WAY
ON ORIGINAL

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ON ORIGINAL