DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022047/S-011/S-016/S-017/S-019/S-022 **SUPPLEMENT APPROVAL**

AstraZeneca
Attention: Pat Patterson
Director, Regulatory Affairs
1800 Concord Pike
P.O. Box 15437
Wilmington, DE 19850-5437

Dear Ms. Patterson:

Please refer to your supplemental new drug application dated February 27, 2008 (S-011) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Seroquel XR (quetiapine fumarate) Extended-Release 50 mg, 150 mg, 200 mg, 300 mg, and 400 mg Tablets.

We acknowledge receipt of your Class 2 resubmission dated June 6, 2009. This submission constituted a complete response to our December 22, 2008 action letter.

This supplemental new drug application (NDA) proposes the following revisions to product labeling:

S-011 (submitted as an efficacy supplement)

- Provides for a new indication of adjunctive therapy in the treatment of Major Depressive Disorder (MDD) and respective labeling changes.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

We also note that your "Changes Being Effected" supplemental applications submitted on July 11, 2008 (S-017), September 11, 2008 (S-019), December 15, 2008 (S-022), and your "Prior Approval" supplement submitted on December 19, 2007 (S-016) have been superseded by this approval action. We will not review these supplemental applications but they will be retained in our files.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling

(text for the package insert). For administrative purposes, please designate this submission, "SPL for approved NDA 22047/S-011".

We request that the revised labeling approved today be available on your website within 10 days of receipt of this letter.

Under 21 CFR 208.24(d), you are responsible for ensuring that the label of each container or package includes a prominent and conspicuous instruction to authorized dispensers to provide a Medication Guide to each patient to whom the drug is dispensed, and states how the Medication Guide is provided. You should submit marked up carton and container labels of all strengths and formulations with the required statement alerting the dispenser to provide the Medication Guide.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for both children and adolescents. At the present time, there are only two approved treatments for pediatric MDD, fluoxetine and escitalopram, both SSRIs. It is not at all clear what the best approach would be for a nonresponding pediatric patient, but most clinicians would not want to move to adding an atypical antipsychotic. Thus, studies of adjunctive therapy in the treatment of Major Depressive Disorder (MDD) would be highly impractical.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

Section 505-1 of the FDCA authorizes FDA to require the submission of a Risk Evaluation and Mitigation Strategy (REMS) if FDA becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)).

Since Seroquel XR (quetiapine fumarate) was approved on May 17, 1997, we have become aware of additional clinical trial data and postmarketing safety data that show a risk of hyperglycemia, hyperlipidemia, and weight gain associated with all forms of Seroquel XR (quetiapine fumarate) in all patient populations. We consider this information to be "new safety information" as defined in section 505-1(b) of FDCA.

Your proposed REMS, submitted on November 24, 2009, and appended to this letter, is approved. The REMS consists of a Medication Guide and a timetable for submission of assessments of the REMS.

The REMS assessment plan should include but is not limited to the following:

a. An evaluation of patients' understanding of the serious risks of SEROQUEL XR (quetiapine fumarate).
b. A report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24.
c. A report on failures to adhere to distribution and dispensing requirements, and corrective actions taken to address noncompliance.

Assessments of an approved REMS must also include, under section 505-1(g)(3)(B) and (C), information on the status of any postapproval study or clinical trial required under section 505 (o) or otherwise undertaken to investigate a safety issue. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)vii) and including any updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

We remind you that in addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in Section 505-1(g)(2)(A) of FDCA.

Prominently identify the submission containing the REMS assessments or proposed modifications with the following wording in bold capital letters at the top of the first page of the submission:

NDA 022047 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 022047
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 022047
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send 5 copies of REMS-related submissions.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) to:

Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

LETTERS TO HEALTH CARE PROFESSIONALS

If you issue a letter communicating important safety related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit an electronic copy of the letter to both this NDA and to the following address:

MedWatch
Food and Drug Administration
5600 Fishers Lane, Room 12B05
Rockville, MD 20857

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, email your Regulatory Project Manager at Juliette.Toure@fda.hhs.gov.

Sincerely,
{See appended electronic signature page}
Thomas Laughren, M.D.
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosures
Content of Labeling
REMS

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22047	SUPPL-11	ASTRAZENECA PHARMACEUTICALS LP	SEROQUEL XR

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

THOMAS P LAUGHREN
12/02/2009