DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-639 S-048

AstraZeneca Pharmaceuticals LP
Attention: Kathryn Bradley
Director, Regulatory Affairs
1800 Concord Pike
P.O. Box 8355
Wilmington, DE 19803-8355

Dear Ms. Bradley:

We acknowledge receipt of your supplemental new drug application dated and received December 4, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Seroquel (quetiapine fumarate) tablets.

This "Changes Being Effected" supplemental new drug application provides for revised labeling to include new safety information for both adult and pediatric patients.

We have no objection to your submission of the new safety information pertaining to the clinical trials as a CBE supplement. However, the Division is requesting that you reformat the information for better integration in the overall label prior to your intended implementation on January 4, 2009. Specifically:

1. Place the pediatric safety information in the relevant sections of labeling with the adult data rather than separately in sections 5.19 and 8.4. For example, the proposed pediatric data in the section 8.4 subtitled "Changes in Thyroid Function Tests" should be placed at the end of section 5.10 (Warnings and Precautions: Hypothyroidism). The same principle applies to other pediatric safety information that already has adult data included prominently.
2. The weight gain signal is significant for both adult and pediatric populations and should be elevated to the Warnings and Precautions section rather than the vital signs section (the latter section could refer back to the information in Warnings and Precautions section) with inclusion of data for both populations. In fact, the data for weight change, glucose changes, and lipid changes from the clinical trials, both adult and pediatric, need to be elevated to the Warnings/Precautions section of labeling. Please see the format used in the currently distributed label for another antipsychotic drug, i.e., Zyprexa, for the correct format for this information.
3. The safety data for Increases in Blood Pressure is an unexpected signal and there is currently no similar adverse event signal for the adult population. Because of this unexpected and clinically significant signal that may be specific to the pediatric population, this safety data should be included in a separate section in Warnings and Precautions. Please offer your rationale for this unusual finding.

4. For each section describing pediatric safety signals, the following statement should be included "Safety and effectiveness of SEROQUEL have not been established in pediatric patients and SEROQUEL is not approved for patients under the age of 18 years".
5. Please replace your proposed Hyperprolactinemia statement with the standard language now used for more recently approved atypical antipsychotic agents, e.g., Invega. Any actual clinical trials data regarding prolactin elevation should, of course, be data for quetiapine, including the pediatric data.
6. All pediatric safety data and the other changes we are requesting for Seroquel should be included in revised labeling for Seroquel XR as well.

The above requested changes should be implemented immediately, and they should be submitted as an amendment to your pending supplemental application to the Seroquel NDA and as an original supplemental application to the Seroquel XR NDA, 22-047, within 30 days from the date of this letter, or notify FDA that you do not believe these changes are warranted, and submit a statement detailing the reasons. If you wish to have our prior comment on your alternative proposal in response to these requests, we would be happy to provide such comment.

Please note that your proposed labeling language in the above referenced CBE is under continuing review by the Agency. Please also note that the Division is currently reviewing your metabolic data submission and the pediatric efficacy supplements submitted under this NDA (S-045 and S-046). We will be providing further labeling comments, if any, and will take final action on these submissions when reviews are completed.

If you have any questions, call Kimberly Updegraff, M.S., Regulatory Project Manager, at 301-796-2201.

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

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

/s/

Thomas Laughren
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