DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-639

AstraZeneca
Attention: Gerald L. Limp
Director Regulatory Affairs
P.O. Box 8355
Wilmington, DE 19803-8255

Dear Mr. Limp:

Please refer to your correspondence dated August 4, 2003, requesting changes to FDA's February 11, 2003, Written Request for pediatric studies for Seroquel (quetiapine fumarate).

We reviewed your proposed changes and are amending the Written Request. The following sections replace the original sections and should be inserted into the Written Request of February 11, 2003. All other terms stated in our Written Request remain the same. Changes are highlighted for ease of review:

1. **Specific Study Requirements for Development Program in Adolescent Schizophrenia**, Study Design, Pediatric Safety Study

   Safety data must be collected in the controlled efficacy trial. In addition, longer- term safety data, for a minimum duration of 6 months exposure to the drug, must be collected. The longer- term safety data could come from open studies, e. g., a longer-term open extension of the controlled efficacy trial populations, from separate longer- term open safety studies, or from controlled studies, e. g., a longer-term safety and efficacy trial. Adequate longer-term safety data from studies in a single indication would be sufficient to meet this requirement. The long- term safety data must be at or above the dose or doses identified as effective in an adequately designed trial, as described above. Since you will not be studying doses below 400 mg/day for effectiveness, any safety experience at doses below 400 mg will not be contributory. Patients that require a dosage decrease, however, should not be dropped from the trial. As long as those patients who receive doses below the minimum dose you establish as effective, or that is perceived in the community as a minimum effective dose, do not exceed 5% of the total, they will not have to be replaced. If an adequately designed and conducted effectiveness trial fails to detect a drug effect, you must still collect long-term safety data, at doses at least as high as the doses typically used in treating patients with this drug.

2. **Timeframe for submitting reports of the study(ies)**

   Reports of the above studies must be submitted to the Agency within 7 years from the date of this letter. Please keep in mind that pediatric exclusivity attaches only to existing patent protection or exclusivity that has not expired at the time you submit your reports of the studies in response to this Written Request.

Reports of the studies that meet the terms of the Written Request dated February 11, 2003, as amended by this letter must be submitted to the Agency on or before February 11, 2010, in order to possibly qualify for pediatric exclusivity extension under Section 505A of the Act.

Submit protocols for the above studies to an investigational new drug application (IND) and clearly mark your submission, **"PEDIATRIC PROTOCOL SUBMITTED FOR PEDIATRIC EXCLUSIVITY STUDY"** in large font, bolded type at the beginning of the cover letter of the submission. Notify us as soon as possible if you wish to enter into a written agreement by submitting a proposed written agreement. Please clearly mark your submission, **"PROPOSED WRITTEN AGREEMENT FOR PEDIATRIC STUDIES"** in large font, bolded type at the beginning of the cover letter of the submission.

Submit reports of the studies as a **supplement to an approved NDA** with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, clearly mark your submission **"SUBMISSION OF PEDIATRIC STUDY REPORTS – PEDIATRIC EXCLUSIVITY DETERMINATION REQUESTED"** in large font, bolded type at the beginning of the cover letter of the submission and include a copy of this letter. In addition, send a copy of the cover letter of your submission, via fax (301-594-0183) or messenger to the Director, Office of Generic Drugs, HFD-600, Metro Park North II, 7500 Standish Place, Rockville, MD 20855-2773.

If you wish to discuss any amendments to this Written Request, submit proposed changes and the reasons for the proposed changes to your application. Clearly mark submissions of proposed changes to this request **"PROPOSED CHANGES IN WRITTEN REQUEST FOR PEDIATRIC STUDIES"** in large font, bolded type at the beginning of the cover letter of the submission. We will notify you in writing if we agree to any changes to this Written Request.

We hope you will fulfill this pediatric study request. We look forward to working with you on this matter in order to develop additional pediatric information that may produce health benefits to the pediatric population.

If you have any questions, call Steven D. Hardeman, R.Ph., Senior Regulatory Project Manager, at (301) 594-5525.

Sincerely,

{See appended electronic signature page}

Robert Temple, M. D.
Director
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/

Robert Temple
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