DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

WRITTEN REQUEST-AMENDMENT 3

NDA 20-579

Boehringer Ingelheim Pharmaceuticals, Inc.
Attention: David R. Brill, Ph.D.
Director, Drug Regulatory Affairs
900 Ridgebury Road
P.O. Box 368
Ridgefield, CT 06877

Dear Dr. Brill:

Please refer to your correspondence dated April 3, 2007, requesting changes to FDA's Written Request for pediatric studies for tamsulosin hydrochloride. This request was originally issued on January 10, 2006, and has subsequently been revised on March 20 and October 18, 2006.

We have reviewed your latest proposed changes and are amending the Study Populations and Study Design sections of your Written Request as shown below. Deleted words are indicated by a ~~strikethrough~~. Added words are indicated by an underline. All other terms in our Written Request issued on January 10, 2006, and as previously amended on March 20 and October 18, 2006, remain the same.

Study Populations, including sample sizes:

Study 1: For the PK/PD characterization, randomize approximately 27 pediatric patients so that there are approximately 9 patients with PK/PD information for each dose level (low, medium, and high). While it is understood that the majority of these patients will be from the low and medium weight categories (i.e. 12.1 – 25 kg and 25.1 – 50 kg), best efforts should be made to obtain PK/PD information from high weight pediatric patients (i.e. 51.0 – 100 kg). ~~approximately 27 patients, so that there are approximately 9 patients with PK/PD information for each dose level (low, medium, and high) and for each body weight category (i.e. 12.1-25 kg, 25.1-50 kg, and 50.1-100 kg~~.

For the long-term safety characterization, enroll a sufficient number of pediatric patients 2 years – 16 years of age with elevated detrusor LPP associated with a known neurological disorder (e.g. spina bifida) to ensure that approximately 75 and 50 patients receive tamsulosin hydrochloride for at least 6 months and 1 year, respectively.

Study 2: Enroll a sufficient number of patients to ensure that approximately 120 pediatric patients 2 years – 16 years of age with elevated detrusor LPP associated with a known neurological disorder (e.g. spina bifida) complete the study, with approximately 30

patients in each dose group (low, medium, and high). Enroll sufficient numbers of patients of each age category (2-< 5 years, 5-<10 years, and 10-16 years) to allow for evaluation of consistency of effects.

Study Design:

Study 1: An open-label study divided into a PK/PD characterization portion, followed by a long-term safety and tolerability portion. The PK/PD portion should include approximately 27 patients who are randomized to low, medium, and high doses. This randomization should be stratified by weight (12.1 – 25 kg, 25.1 – 50 kg, and 50.1 – 100 kg). Day 1 pharmacokinetics should be characterized at the low dose in patients who are reasonably distributed across the three body weight categories. Tamsulosin steady-state pharmacokinetics should be assessed in all patients when they finish 2 weeks of treatment on their final randomized dose level (i.e. on Day 14, 21, and 28 for the low, medium, and high dose groups, respectively). When the PK portion of the trial is completed, the PK/PD and safety information should be shared with the Agency for our review. In addition, a comparison of the target pediatric exposure data against existing adult data should be provided in this report**.** The study may continue enrolling new patients in parallel to the sponsor's submission and FDA review of the interim PK/PD and safety report~~. Except for the first 27 patients who may continue in the study, no additional patients will be treated until the Agency has formally agreed that it is acceptable to do so. The sponsor must receive a formal statement from the Agency that patients who did not participate in the PK/PD portion of the study may begin treatment, increasing doses according to the individual's efficacious dose level.~~

Study 2: A randomized, double-blind, placebo-controlled, safety and efficacy study. The randomization to placebo, low, medium, or high dose groups should be stratified by: location of study centre (North America or Europe), age group (2-<5 years, 5-<10 years, and 10-16 years), and concomitant use of anti-cholinergic medication. The study should have a dose-titration lead-in phase and a 12-week maintenance phase. This study may be initiated in parallel to the sponsor's submission and the FDA review of the interim PK/PD and safety report from Study 1. ~~This study may not be initiated until the preliminary PK/PD and safety information from approximately 27 patients from Study 1 have been assessed by the Agency, and the sponsor has been informed that it is acceptable to continue Study 1 and to initiate Study 2.~~

Reports of the studies that meet the terms of the Written Request dated January 10, 2006, as amended by this letter and the letters issued on March 10 and October 18, 2006, must be submitted to the Agency on or before July 1, 2009, 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 new drug application (NDA) or as a supplement to your 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 Olga, Salis, Regulatory Health Project Manager, at (301) 796-0837.

Sincerely,

{See appended electronic signature page}

Julie Beitz, M.D.
Director
Office of Drug Evaluation III
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/

Julie Beitz
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