DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-771
NDA 21-228

Pharmacia & Upjohn Company
Attention: Gregory G. Shawaryn
Regulatory Manager, Regulatory Affairs
7000 Portage Road
Kalamazoo, MI 49001-0199

Dear Mr. Shawaryn:

Reference is made to your correspondence dated April 9, 2002, June 14, 2002, and July 15, 2002 requesting changes to FDA's January 23, 2001, Written Request for pediatric studies for tolterodine tartrate tablets.

We have reviewed your proposed changes and are amending the below listed sections of the Written Request. All other terms stated in our Written Request issued on January 23, 2001 and amended on November 15, 2001 remain the same.

Study #1, Drug Information:

We agree with your request to change this section to correlate to doses employed in Protocol 583E-URO-0581-001.

Therefore, we are amending the sentence that currently reads as follows:

> "The patient's clinician will select the appropriate total daily dose for each patient within the range of 0.2-2.0 mg that will be administered orally in divided doses."

to

> "The total daily dose for each patient will be administered orally in divided doses and will follow a sequential dose escalation design, with each patient serving as his/her own control, increasing through three dosage levels: 0.03 mg/kg/day for 4 weeks, 0.06 mg/kg/day for four weeks, and 0.12 mg/kg/day for four weeks."

Study #1, Timeframe for submitting reports of the study:
We agree to extend the timeframe for submitting a report of this study by three months.

Therefore, we are amending the sentence that currently reads as follows:

"A report of the above study must be submitted to the Agency on or before December 15, 2002."

to:

"A report of the above study must be submitted to the Agency on or before March 15, 2003."

Study #2, Drug Information:

We agree with your request to change the section to correlate to doses employed in Protocol 583E-URO-0581-002.

Therefore, we are amending the sentence that currently reads as follows:

"The patient's clinician will select the appropriate total daily dose for each patient within the range of 0.5-4 mg that will be administered orally in divided doses."

to

"The total daily dose for each patient will be administered orally in divided doses and will follow a sequential dose escalation design, with each patient serving as his/her own control, increasing through three dosage levels: 0.03 mg/kg/day for 4 weeks, 0.06 mg/kg/day for four weeks, and 0.12 mg/kg/day for four weeks."

Study #2, Timeframe for submitting reports of the study:
We agree to extend the timeframe for submitting a report of this study by three months.

Therefore, we are amending the sentence that currently reads as follows:

"A report of the above study must be submitted to the Agency on or before December 15, 2002."

to:

"A report of the above study must be submitted to the Agency on or before March 15, 2003."

Study #3, Drug Information:

We agree with your request to change the section to correlate to doses employed in Protocol 583E-URO-0581-003.

Therefore, we are amending the sentence that currently reads as follows:

"The patient's clinician will select the appropriate total daily dose for each patient within the range of 2-4 mg. The dose will be administered orally once daily."

to

> "The total daily dose for each patient will be administered orally in divided doses and will follow a sequential dose escalation design, with each patient serving as his/her own control, increasing through three dosage levels: 2 mg/day for 4 weeks, 4 mg/kg/day for four weeks, and 6 mg/kg/day for four weeks."

Study #3, Timeframe for submitting reports of the study:
We agree to extend the timeframe for submitting a report of this study by three months.

Therefore, we are amending the sentence that currently reads as follows:

> "A report of the above study must be submitted to the Agency on or before December 15, 2002."

to:

> "A report of the above study must be submitted to the Agency on or before March 15, 2003."

Study #4, Timeframe for submitting reports of the study:
We agree with your request to change the timeframe for submitting reports of this study by three months.

Therefore, we are amending the sentence that currently reads as follows:

> "A report of the above study must be submitted to the Agency on or before December 15, 2002."

to:

> "A report of the above study must be submitted to the Agency on or before March 15, 2003."

Reports of the studies that meet the terms of the Written Request dated January 23, 2001, as amended by this letter and the amendment dated November 15, 2001 must be submitted to the Agency on or before March 15, 2003, 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, contact Jen Mercier, Regulatory Project Manager, at 301-827-4260.

Sincerely,

Victor Raczkowski, M.D., M.S.
Deputy 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/

Victor Raczkowski
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