DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-228

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

Dear Mr.Shawaryn:

Please refer to your new drug application (NDA) dated February 25, 2000, received February 29, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Detrol LA (tolterodine extended release) 2 and 4 mg capsules.

We acknowledge receipt of your submissions dated February 25, March 31, April 3, May 17, June 28, 30, October 25, 30, November 3, 13, 15, December 7, 15 and 21, 2000.

This new drug application provides for the use of Detrol LA (tolterodine extended release) 2 and 4 mg capsules for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency and frequency.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the attached labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert submitted December 21, 2000, immediate container and carton labels submitted December 15, 2000). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999). For administrative purposes, this submission should be designated "FPL for approved NDA 21-228." Approval of this submission by FDA is not required before the labeling is used.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). Reference is made to your proposed pediatric drug development plan and Proposed Pediatric Study Request (PPSR) for tolterodine extended release, submitted as Amendment #5 to NDA 21-228 on June 28, 2000. We have reviewed your proposed pediatric drug development plan. We remind you of our November 29, 2000 teleconference where we notified you of the tolterodine extended release Pediatric Study Requirements under the Pediatric Rule. In the November 29, 2000, teleconference you agreed to attempt to develop a tolterodine syrup formulation for study in pediatric patients. In addition, we notified you that the pediatric study requirement for the age group of neonate (birth to one month) was waived, and that studies in the age group of one month to fifteen years were deferred until December 15, 2002.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at www.fda.gov/cder/pediatric) for details. FDA generally will not accept studies submitted to an NDA before issuance of a Written Request as responsive to a Written Request. Sponsors should obtain a Written Request before submitting pediatric studies to an NDA. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity. FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as it does to fulfill the requirements of the pediatric rule.

We remind you that validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Evelyn R. Farinas, R.Ph., M.G.A., Regulatory Project Manager, at (301) 827-4260.

Sincerely,

Susan Allen, M.D.
Director
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research