

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER: 20-771/S-004

APPROVABLE LETTER

NDA 20-771/S-004

OCT 23 2000

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

Dear Mr. Shawaryn:

Please refer to your supplemental new drug application dated December 22, 1999, received December 23, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Detrol (tolterodine tartrate) tablets.

We acknowledge receipt of your submissions dated May 5, July 14, August 28, and September 21, 2000.

This supplemental new drug application proposes the use of Detrol (tolterodine tartrate) tablets for treatment of patients with an overactive bladder with symptoms of urinary frequency, urgency and urge incontinence.

We have completed the review of this application, as amended, and it is approvable. Before this application may be approved, however, it will be necessary for you to submit draft labeling revised in accordance with the enclosed labeling. Approval of this application is also dependent on satisfactory completion of the Division of Scientific Investigations' inspection of all study sites.

In addition, all previous revisions as reflected in the most recently approved labeling must be included. To facilitate review of your submission, please provide a highlighted or marked-up copy that shows the changes that are being made.

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

Under 21 CFR 314.50(d)(5)(vi)(b), we request that you update your NDA by submitting all safety information you have regarding your new drug. Please provide updated information as listed below. The update should cover all studies and uses of the drug including: (1) those involving indications not being sought in the present submission, (2) other dosage forms, and (3) other dose levels, etc.

1. Retabulation of all safety data including results of trials that were still ongoing at the time of NDA submission. The tabulation can take the same form as in your initial submission. Tables comparing adverse reactions at the time the NDA was submitted versus now will certainly facilitate review.

2. Retabulation of drop-outs with new drop-outs identified. Discuss, if appropriate.
3. Details of any significant changes or findings.
4. Summary of worldwide experience on the safety of this drug.
5. Case report forms for each patient who died during a clinical study or who did not complete a study because of an adverse event.
6. English translations of any approved foreign labeling not previously submitted.
7. Information suggesting a substantial difference in the rate of occurrence of common, but less serious, adverse events.

Within 10 days after the date of this letter, you are required to amend the supplemental application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

This product may be considered to be misbranded under the Federal Food, Drug, and Cosmetic Act if it is marketed with these changes prior to approval of this supplemental application.

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

Sincerely,

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

Enclosure

cc:

Archival NDA 20-771

HFD-580/Div. Files

HFD-580/E.Farinas

HFD-580/Allen/Shames/Hirsch/Gierhart/Parekh/Chatterjee/Jordan/Lin/Rhee/Kammerman/
Hoberman/Rumble

HFD-002/ORM

HFD-103/ADRA

HFD-42/DDMAC (with labeling)

DISTRICT OFFICE

Drafted by: erf/October 23, 2000

Initialed by:

Allen/Shames/Hirsch/Gierhart/Jordan/Parekh/Chatterjee/Lin/Rhee/Kammerman/Hoberman/
Rumble

final: erf/ 10.23.00

filename: NDA 20771 S004 approvable letter October.doc

APPROVABLE (AE)

Concurrence		
Name/Title	Signature	Date
Evelyn R. Farinas, R. Ph., M.G.A Regulatory Project Manager	/s/	10-23-00
Terri Rumble, B.S.N. Chief, Project Management Staff		10/23/00
Brenda Gierhart, M.D. Medical Officer		10/23/00
Mark Hirsch, M.D. <i>Medical Officer</i> Acting Urology Team Leader		10/23/00
David Hoberman, Ph.D. Statistics Reviewer		2/23/00
Lisa Kammerman, Ph.D. Team Leader, Statistics		10/23/00
David Lin, Ph.D. Chemistry Reviewer		1/23/00
Moo-Jhong Rhee, Ph.D. Team Leader, Chemistry		1/23/00
D.J. Chatterjee, Ph.D. Clinical Pharmacology and Biopharmaceutics Reviewer		1/23/00
Ameeta Parekh, Ph.D. Team Leader, Clinical Pharmacology and Biopharmaceutics		1/23/00
Daniel Shames, M.D. Acting Deputy Director		1/23/00
Susan Allen, M.D. Director		10/23/00

137 page(s) of
revised draft labeling
has been redacted
from this portion of
the review.
