CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-228 S-006

CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW
OF **SUPPLEMENT**

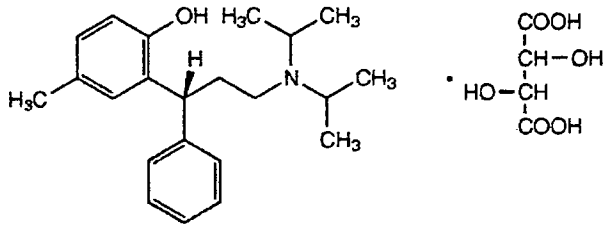
1. **ORGANIZATION:** DRUDP HFD-580
2. **NDA NUMBER:** 21-228
3. **SUPPLEMENT NUMBER/DATES:** SE8-006
   Letterdate: 10-OCT-2003
   Stampdate: 14-OCT-2003
4. **AMENDMENTS/REPORTS/DATES:**
5. **RECEIVED BY CHEMIST:** 17-NOV-2003

6. **APPLICANT NAME AND ADDRESS:**
   Pharmacia & Upjohn Co.
   7000 Portage Road
   Kalamazoo MI 49001

7. **NAME OF DRUG:**
   Detrol LA

8. **NONPROPRIETARY NAME:**
   Tolterodine tartrate extended release capsules

9. **CHEMICAL NAME/STRUCTURE:**
   (R)-N,N-diisopropyl-3-(2-hydroxy-5-methylphenyl)-3-phenylpropanamine L-hydrogen tartrate



10. **DOSAGE FORM(S):**
    extended release capsules

11. **POTENCY:**
    2 mg and 4 mg

12. **PHARMACOLOGICAL CATEGORY:**
    Treatment of overactive bladder

13. **HOW DISPENSED:**
    Rx

14. **RECORDS & REPORTS CURRENT:**
    None

15. **RELATED IND/NDA/DMF:**
    None

16. **SUPPLEMENT PROVIDES FOR:**
Pediatric studies as requested by FDA in the 23-JAN-2001 Written Request letter.

17. **COMMENTS:**

- NDA 21-228 SE8 is submitted in response to the Written Request for Pediatric Studies issued by FDA on 23-JAN-2001. This efficacy supplement is submitted with data from 10 clinical studies in order for the applicant to obtain the pediatric exclusivity described in the Written Request. The CMC section of the supplement consists of only composition information on the clinical batches used in the pediatric studies. These batches include the currently approved extended release capsules and the immediate release tablets, as well as an investigational oral solution. The applicant references the currently approved NDAs 21-228 and 20-771 for all chemistry information on the extended release capsules and the immediate release tablets. The applicant does not intend to market the oral solution that was used in 3 of the 10 clinical studies. There is **no change to the Description, Dosage, and How Supplied sections of the currently approved physician insert**. Therefore, because **there is no new formulation proposed for commercial distribution**, the reference to chemistry information on the currently approved products of NDAs 21-228 and 20-771 is adequate, and the composition information on the investigational oral solution is adequate for the purpose of the investigation studies.
- Refer to the attached Chemist's Review Notes for details.

18. **CONCLUSIONS AND RECOMMENDATIONS:**
All chemistry information provided in the supplement SE8-006 is adequate. From the Chemistry perspective, the supplement is recommended for approval.

19. **REVIEWER NAME** **SIGNATURE** **DATE COMPLETED**
Suong T. Tran, Ph.D.

cc:
Original: NDA 21-228
HFD-580/Division File
HFD-580/JKing
HFD-580/STran/MJRhee

INIT by MJ Rhee

Filename: 21228 SE8-006.doc

1 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Chemist Review Notes

1 page

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Suong Tran
12/15/03 04:30:29 PM
CHEMIST

paper sign-off 12/15/03

Moo-Jhong Rhee
12/15/03 04:36:28 PM
CHEMIST
I concur

CHEMISTRY NDA FILEABILITY CHECKLIST

NDA: 21-228 SE8/006
Applicant: Pharmacia & Upjohn Co.
Letter Date: 10-OCT-2003

Drug Name: Detrol LA Capsules (tolterodine extended release capsules)

IS THE CMC SECTION OF APPLICATION FILEABLE? Yes

The following parameters are necessary in order to initiate a full review, i.e., complete enough to review but may have deficiencies.

	Parameter	Yes	No	Comment
1	On its face, is the section organized adequately?	X		
2	Is the section indexed and paginated adequately?	X		
3	On its face, is the section legible?	X		
4	Are ALL of the facilities (including contract facilities and test laboratories) identified with full street addresses and CFNs?		X	
5	Is a statement provided that all facilities are ready for GMP inspection?		X	
6	Has an environmental assessment report or categorical exclusion been provided?		X	
7	Does the section contain controls for the drug substance?		X	
8	Does the section contain controls for the drug product?		X	
9	Have stability data and analysis been provided to support the requested expiration date?		X	
10	Has all information requested during the IND phase, and at the pre-NDA meetings been included?		X	
11	Have draft container labels been provided?		X	
12	Has the draft package insert been provided?	X		
13	Has an investigational formulations section been provided?	X		
14	Is there a Methods Validation package?		X	
15	Is a separate microbiological section included?		X	Solid oral dosage form.

Comments:

- Even though there is a lack of chemistry information as indicated in the table above, NDA 21-228 SE8 is acceptable for filing for the following reason:

  NDA 21-228 SE8 is submitted in response to the Written Request for Pediatric Studies issued by DRUDP on 23-JAN-2001. This efficacy supplement is submitted with data from 10 clinical studies in order for the applicant to obtain the pediatric exclusivity described in the Written Request. The CMC section of the supplement consists of only composition information on the clinical batches used in the pediatric studies. These batches include the currently approved extended release capsules and the immediate release tablets, as well as an investigational oral solution. The applicant references the currently approved NDAs 21-228 and 20-771 for all chemistry information on the extended release capsules and the immediate release tablets. The applicant does not intend to market the oral solution that was used in 3 of the 10 clinical studies. There is no change to the Description, Dosage, and How Supplied sections of the currently approved physician insert. Therefore, because there is no new formulation proposed for commercial distribution, the reference to chemistry information on the currently approved products of NDAs 21-228 and 20-771 is adequate, and the composition information on the investigational oral solution is adequate for the purpose of the investigation studies.

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Suong Tran
11/26/03 03:03:15 PM
CHEMIST

Moo-Jhong Rhee
12/1/03 10:01:03 AM
CHEMIST
I concur

NDA 21-228/S006 Detrol LA
tolterodine tartrate extended release capsules, 2 and 4 mg

Drug Master File (DMF)

Not applicable. No new CMC information was submitted in this supplemental application.

NDA 21-228/S006 Detrol LA
tolterodine tartrate extended release capsules, 2 and 4 mg

Methods Validation

Not applicable. No new CMC information was submitted in this supplemental application.