CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

20-597/S026

Trade Name: Xalatan

Generic Name: Latanprost

Sponsor: Pharmacia and Upjohn

Approval Date: 11/15/2002

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-597/S026

CONTENTS

Reviews / Information Included in this NDA Review.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-597/S026

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-597/S-026

Pharmacia & Upjohn Company
Attention: Diane M. Gremban
Senior Regulatory Manager
7000 Portage Road
Kalamazoo, Michigan 49001

Dear Ms. Gremban:

Please refer to your supplemental new drug application dated July 12, 2002, received July 15, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Xalatan (latanoprost ophthalmic solution) 0.005%.

This supplemental new drug application provides for an alternate drug product manufacturing process in a new line at Automatic Liquid Packaging, Woodstock, Illinois.

We have completed the review of this supplemental application, and it is approved.

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 Michael Puglisi, Project Manager, at (301) 827-2090.

Sincerely,

{See appended electronic signature page}

Linda L. Ng, Ph.D.
Chemistry Team Leader for the
Division of Anti-Inflammatory, Analgesic and
Ophthalmic Drug Products, HFD-550
DNDC III, Office of New Drug Chemistry
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/

Linda Ng

11/15/02 03:33:58 PM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-597/S026

CHEMISTRY REVIEW(S)

Chemistry Review #2	**1. Division** HFD-550	**2. NDA Number** 20-597
3. Name and Address of Applicant Pharmacia & Upjohn 7000 portage Rd. Kalamazoo, MI 49001	**4. Supplement** **Number** SCM-026 **Letter Date** 7/12/02 **Stamp Date** 7/15/02 **Due Date**	
5. Name of Drug Xalatan	**6. Nonproprietary Name** Latanoprost Ophthalmic Solution	
7. Supplement Provides for: An alternate manufacturing process in a new line for the drug product at ALP ,Woodstock, IL. This is a PA supplement		**8. Amendment(s)**
9. Pharmacological Category Anti-hypertensive	**10. How Dispensed** ℞	**11. Related Documents** FDA e-mail dated 8//12/02 and 8/28/02
12. Dosage Form Solution	**13. Potency(ies)** 0.005%	

14. Chemical Name and Structure see USAN

15. Comments

The application was approved on 6/5/96.

The supplement proposed an addition of an alternate manufacturing process (b) (4) In addition the approved manufacturing process will be changed when used (b) (4). The primary differences were discussed in chemist's review #1 dated 10/21/02. The supplement was in "approvable" status pending for a satisfactory microbiology review (b) (4) Microbiologist review is complete and the application is recommended for "Approval".

16. Conclusions and Recommendations

application is recommended for approval from a chemistry, manufacturing & control standpoint.

17. Name	**Signature**	**Date**
Su C. Tso, Ph.D.		11/13/02

Concurrence
Linda Ng, Ph.D., Team Leader

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

/s/

Su Tso
11/13/02 02:09:52 PM
CHEMIST

Linda Ng
11/14/02 08:50:47 AM
CHEMIST
PM to prepare AP letter

Chemistry Review #1	**1. Division** HFD-550	**2. NDA Number** 20-597
3. Name and Address of Applicant Pharmacia & Upjohn 7000 portage Rd. Kalamazoo, MI 49001	**4. Supplement** **Number** SCM-026 **Letter Date** 7/12/02 **Stamp Date** 7/15/02 **Due Date**	
5. Name of Drug Xalatan	**6. Nonproprietary Name** Latanoprost Ophthalmic Solution	
7. Supplement Provides for: an alternate manufacturing process in a new line for the drug product at ALP ,Woodstock, IL. This is a PA supplement		**8. Amendment(s)**
9. Pharmacological Category Anti-hypertensive	**10. How Dispensed** ℞	**11. Related Documents** FDA e-mail dated 8//12/02 and 8/28/02
12. Dosage Form Solution	**13. Potency(ies)** 0.005%	

14. Chemical Name and Structure see USAN

15. Comments

The application was approved on 6/5/96.

The supplement proposed an addition of an alternate manufacturing process (b) (4) In addition the approved manufacturing process will be changed when used (b) (4) The primary differences in the two processes are:

(b) (4)

For detail, refer to REVIEWER NOTES.

Process validation is consulted to microbiologist for review

The addition of the (b) (4) .

Automatic Liquid Packaging was inspected on 3/5/01, District recommended, on 4/24/01, "withhold" of the application due to validation failure. New EES is requested on 7/20/02. Currently the manufacturing site at ALP (b) (4) in GMP compliance as of 9/25/02.

16. Conclusions and Recommendations

application is recommended for approval from a chemistry, manufacturing & control standpoint However, the final approval is pnding for a satisfactory microbiology review.

17. Name	**Signature**	**Date**
Su C. Tso, Ph.D.		10/21/02

Concurrence
Linda Ng, Ph.D., Team Leader

__7____ Page (s) Withheld

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

____ § 552(b)(4) Draft Labeling

____ § 552(b)(5) Deliberative Process

Withheld Track Number: Chemistry-20-597/S026

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

/s/

Su Tso
10/21/02 01:14:47 PM
CHEMIST

The final approval is pending for a satisfactory microbiology review

Linda Ng
10/21/02 04:41:46 PM
CHEMIST
Micro review is pending

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-597/S026

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review
Review for HFD-550

October 22, 2002

NDA: 20-597/SCS-026

Drug Product Name
Proprietary: XALATAN™
Non-proprietary: Latanoprost Ophthalmic Solution
Drug Product Classification: Topical Ophthalmic

Review Number: 1

Subject of this Review
Submission Date: 7/12/02
Receipt Date: 7/15/02
Consult Date: 7/18/02
Date Assigned for Review: 8/23/02

Applicant/Sponsor
Name: Pharmacia & Upjohn Co.
Address: 7000 Portage Road
Kalamazoo, MI 49001-4000
Representative: Diane Gremban
Telephone: (616) 833-8237

Name of Reviewer: James L. McVey

Conclusion: This supplement requesting (b) (4) the manufacture of latanoprost ophthalmic solution for Pharmacia & Upjohn is recommended for approval from a product quality microbiology perspective.

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUPPLEMENT: Prior Approval

2. SUPPLEMENT PROVIDES FOR: (b) (4) [redacted]

3. MANUFACTURING SITE: Automatic Liquid Packaging
2200 Lake Shore Drive
Woodstock, IL. 60098

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: Eyedrop, 0.005% (50 µg/mL). One drop contains about 1.5 µg latanoprost. The fill volume is 2.5 mL.

5. METHOD(S) OF STERILIZATION: (b) (4) [redacted]

6. PHARMACOLOGICAL CATEGORY: A selective prostanoid FP receptor agonist.

B. SUPPORTING/RELATED DOCUMENTS: n.a.

C. REMARKS: (b) (4) [redacted]

filename: 20597s26r1

Executive Summary

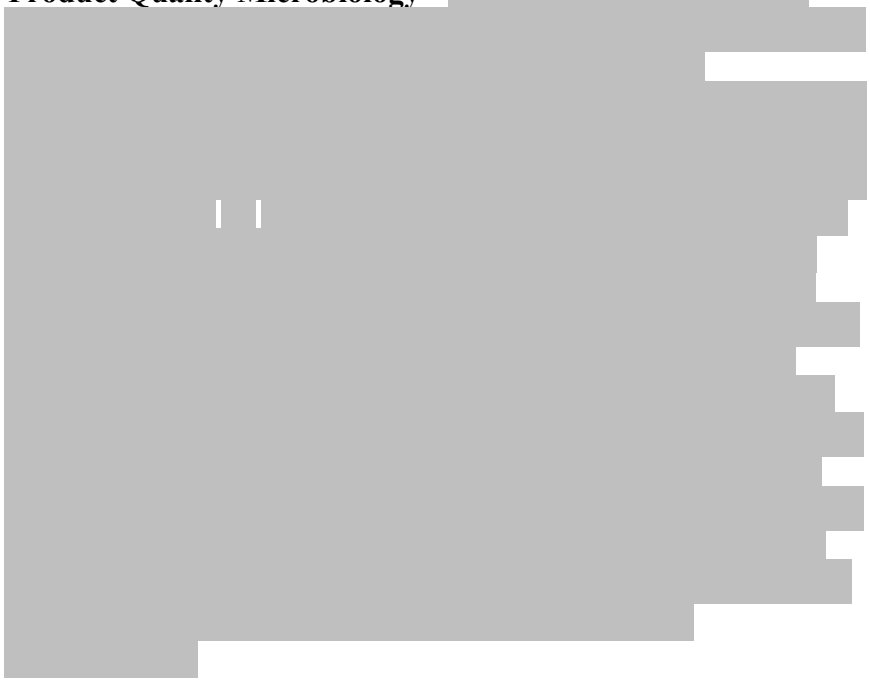
I. Recommendations

A. Recommendation on Approvability – The supplement is recommended for approval from a product quality microbiology standpoint.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable – n.a.

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology – (b) (4)



B. Brief Description of Microbiology Deficiencies – n.a.

C. Assessment of Risk Due to Microbiology Deficiencies – No deficiencies were found so the risk is minimal.

III. Administrative

A. Reviewer's Signature _____

B. Endorsement Block

Microbiologist. James L. McVey
Microbiology Supervisor. Peter Cooney

C. CC Block

HFD- 805/Division File/20597S26r1

___6___ Page (s) Withheld

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

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: ProdMicb-20-597/S026

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

/s/

James McVey
11/13/02 07:01:27 AM
MICROBIOLOGIST

Peter Cooney
11/13/02 09:43:36 AM
MICROBIOLOGIST

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-597/S026

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADM NISTRATION

REQUEST FOR CONSULTATION

TO *(Division/Office)*:	FROM:
Peter Cooney / HFD-805	**Mike Puglisi, Project Manager HFD-550**

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
July 18, 2002		20-597/S-026	CMC Supplement	July 12, 2002

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Xalatan Ophthalmic Solution			October 15, 2002

NAME OF FIRM: Pharmacia & Upjohn

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE--NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☐ OTHER *(SPECIFY BELOW)*:

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

Peter-

Please provide a micro review for this cmc supplement. It provides for a new manufacturing process in (b) (4) (b) (4) This is a paper submission. I'll send the jackets (2 volumes) to you through the document room. Please let me know if I can assist your staff's review in any way. Thanks.

-Mike

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one) ☐ MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

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

/s/

Michael Puglisi

7/18/02 04:59:58 PM