CENTRAL 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
## CONTENTS

Reviews / Information Included in this NDA Review.

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<td>Approval Letter</td>
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<td>Administrative/Correspondence Document(s)</td>
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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
20-597/S026

APPROVAL LETTER
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,

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/
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Linda Ng
11/15/02 03:33:58 PM
<table>
<thead>
<tr>
<th>Chemistry Review #2</th>
<th>1. Division HFD-550</th>
<th>2. NDA Number 20-597</th>
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<tbody>
<tr>
<td>3. Name and Address of Applicant</td>
<td>4. Supplement Number SCM-026</td>
<td>Letter Date 7/12/02</td>
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<tr>
<td>Pharmacia &amp; Upjohn</td>
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<tr>
<td>7000 portage Rd.</td>
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<tr>
<td>Kalamazoo, MI 49001</td>
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<tr>
<td>5. Name of Drug Xalatan</td>
<td>6. Nonproprietary Name Latanoprost Ophthalmic Solution</td>
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<td>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</td>
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<td>8. Amendment(s)</td>
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<td>9. Pharmacological Category Anti-hypertensive</td>
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<tr>
<td>10. How Dispensed Solution</td>
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<tr>
<td>11. Related Documents FDA e-mail dated 8/12/02 and 8/28/02</td>
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<td>12. Dosage Form Solution</td>
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<tr>
<td>13. Potency(ies) 0.005%</td>
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<tr>
<td>14. Chemical Name and Structure see USAN</td>
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<tr>
<td>15. Comments The application was approved on 6/5/96. The supplement proposed an addition of an alternate manufacturing process. In addition the approved manufacturing process will be changed when used . 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 Microbiologist review is complete and the application is recommended for “Approval”.</td>
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<tr>
<td>16. Conclusions and Recommendations application is recommended for approval from a chemistry, manufacturing &amp; control standpoint.</td>
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<tr>
<td>17. Name Su C. Tso, Ph.D.</td>
<td>Signature</td>
<td>Date 11/13/02</td>
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<tr>
<td>Concurrence Linda Ng, Ph.D., Team Leader</td>
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/s/
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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
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<th><strong>1. Division</strong></th>
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<td>For detail, refer to REVIEWER NOTES.</td>
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<td>Process validation is consulted to microbiologist for review</td>
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<td>The addition of the</td>
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<tr>
<td>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 in GMP compliance as of 9/25/02.</td>
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<td><strong>16. Conclusions and Recommendations</strong></td>
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/s/
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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 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:

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:

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

B. SUPPORTING/RELATED DOCUMENTS: n.a.

C. REMARKS:

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

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

TO (Division/Office):

Peter Cooney / HFD-805

FROM:

Mike Puglisi, Project Manager  HFD-550

DATE

July 18, 2002

IND NO.

NDA NO.

20-597/S-026

TYPE OF DOCUMENT

CMC Supplement

DATE OF DOCUMENT

July 12, 2002

NAME OF DRUG

Xalatan Ophthalmic Solution

PRIORITY CONSIDERATION

CLASSIFICATION OF DRUG

DESIRED COMPLETION DATE

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

☐ BIOAVAILABILITY 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) 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
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/s/
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Michael Puglisi
7/18/02 04:59:58 PM