

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**Approval Package for:**

***APPLICATION NUMBER:***

**20-597/S005**

***Trade Name:*** Xalatan

***Generic Name:*** Latanprost

***Sponsor:*** Pharmacia and Upjohn

***Approval Date:*** 7/31/1998

# CENTER FOR DRUG EVALUATION AND RESEARCH

**APPLICATION NUMBER:  
20-597/S005**

## CONTENTS

### Reviews / Information Included in this NDA Review.

<b>Approval Letter</b>	✓
<b>Other Action Letters</b>	
<b>Labeling</b>	
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<b>Summary Review</b>	
<b>Officer/Employee List</b>	
<b>Office Director Memo</b>	
<b>Cross Discipline Team Leader Review</b>	
<b>Medical Review(s)</b>	
<b>Chemistry Review(s)</b>	✓
<b>Environmental Assessment</b>	
<b>Pharmacology Review(s)</b>	
<b>Statistical Review(s)</b>	
<b>Microbiology Review(s)</b>	✓
<b>Clinical Pharmacology/Biopharmaceutics Review(s)</b>	
<b>Other Reviews</b>	
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<b>Proprietary Name Review(s)</b>	
<b>Administrative/Correspondence Document(s)</b>	✓

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**20-597/S005**

**APPROVAL LETTER**

Food and Drug Administration  
Rockville MD 20857

NDA 20-597/S-005

Pharmacia & Upjohn Company  
Attention: Daniel G. Mannix, Ph.D.  
Director, Regulatory Affairs  
7000 Portage Road  
Kalamazoo, Michigan 49001

JUL 31 1998

Dear Dr. Mannix:

Please refer to your March 19, 1998, supplemental new drug application, received March 20, 1998, submitted under section 505 (b) of the Federal Food, Drug, and Cosmetic Act for XALATAN™ (latanoprost ophthalmic solution) Sterile Ophthalmic Solution.

We note that this supplement was submitted as a "Special Supplement - Changes Being Effected" under 21 CFR 314.70(c). However, as we notified you in our March 30, 1998, letter to this application, the proposed change is not the kind of change permitted by regulation to be put into effect prior to approval of a supplement. Therefore, the supplement was reviewed under 21 CFR 314.70(b).

The supplemental application provides for a change in the contract sterilizing facility of caps and tips.

We have completed the review of this supplemental application and it is approved effective on the date of this letter.

This approval affects only the change specifically submitted in this supplemental application. Other changes that may have been approved or are pending evaluation are not affected.

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 please contact Raphael R. Rodriguez, Project Manager, at (301) 827-2090.

Sincerely,

*Hasmukh B. Patel 7-31-98*

Hasmukh B. Patel, Ph.D.  
Chemistry Team Leader, DNDC III  
Division of Anti-Inflammatory, Analgesic, and  
Ophthalmic Drug Products, HFD-550  
Office of Drug Evaluation V  
Center for Drug Evaluation and Research

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cc:

NDA 20-597

HFD-550/Div. Files

HFD-550/DepDir/Chambers *WMA < 7/31/98*

HFD-550/TLChem/Patel

HFD-550/CSO/Rodriguez *RJR 7/23/98*

HFD-550/Chem/Tso *GL 7/21/98*

HFD-830/Chen

HFD-105

HFD-95

DISTRICT OFFICE

saved as: n:\rodrigue\pharmacia\20597s05ap

APPROVAL (AP)

REC 2

**CENTER FOR DRUG EVALUATION AND  
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*APPLICATION NUMBER:*

**20-597/S005**

**CHEMISTRY REVIEW(S)**

DF

JUN 26 1998

DIVISION OF ANTI-INFLAMMATORY, ANALGESIC  
AND OPHTHALMIC DRUG PRODUCTS

Review of Chemistry, Manufacturing, and Controls

**NDA #:** 20-597 **CHEM.REVIEW #:** S-005 **REVIEW DATE:** 4/30/98

<u>SUBMISSION/TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
scs	3/14/98	3/20/98	3/30/98

**NAME & ADDRESS OF APPLICANT:** Pharmacia & Upjohn  
Kalamazoo, MI 49001-0199

**DRUG PRODUCT NAME**

<u>Proprietary:</u>	Xalatan
<u>Nonproprietary/USAN:</u>	Latanoprost
<u>Code Names/ #'s:</u>	PHXA41, XA41
<u>Chemical Type/</u>	1 P
<u>Therapeutic Class:</u>	prostaglandin

**PHARMACOLOGICAL CATEGORY/INDICATION:**

Prostaglandin, Anti-hypertensive/glaucoma

**DOSAGE FORM:** Sterile solution

**STRENGTHS:** 0.005% or 50 ug/mL

**ROUTE OF ADMINISTRATION:** Topical/Ocular

**DISPENSED:**  Rx  OTC

**CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA,  
MOL.WT:**

Chemical Name:

**RELATED DOCUMENT:**

DMI (b) (4) letter of authorization dated 3/1/98 (b) (4)

NDA 20-597  
Pharmacia & Upjohn  
Xalatan (latanoprost), 0.5%

page 2

REMARKS/COMMENTS:

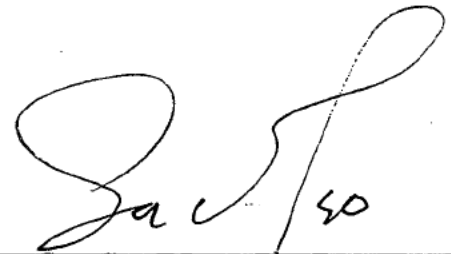
The NDA approved sterilization facility was (b)(4)  
(b)(4) The firm requests to transfer the  
sterilization facility to

(b)(4)  
A letter of authorization dated 3/4/98 was provided in the  
supplement. Summary of validation studies to qualify the  
sterilization process at (b)(4) has  
been forwarded to Peter Cooney for review. There is no  
related chemistry to be reviewed.

The site is in GMP compliance as of 4/23/98. Compliance's  
statement is attached. Microbiologist recommends approval.  
Micro review report attached.

CONCLUSIONS & RECOMMENDATIONS:

The application is recommended for approval from a chemistry  
standpoint.



Su C. Tso, Ph.D  
Review chemist

cc: Orig. NDA 20-597  
HFD-550/Division File  
HFD-830/Chen  
HFD-550/Tso  
HFD-550/Chambers  
HFD-550/Gonzalez Rodriguez  
HFD-550/Patel

Hasmuleh B. Patel  
6/26/98

Microbiologist  
Approved  
7/27/98  
Recommended  
scT



CDER Establishment Evaluation Report  
for April 29, 1998

Page 1 of 1

Application: NDA 20597/005  
Stamp: 20-MAR-1998 Regulatory Due: 20-SEP-1998  
Applicant: PHARMACIA AND UPJOHN  
7000 PORTAGE RD  
KALAMAZOO, MI 490010199

Priority: 1P  
Action Goal:  
Brand Name: XALATAN (LATANOPROST)STERILE  
OPHTHALMIC

Org Code: 550  
District Goal: 16-JUL-1998

Established Name:  
Generic Name: LATANOPROST  
Dosage Form: LIQ (LIQUID)  
Strength: 0.005%

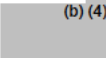
FDA Contacts: L. GORSKI (HFD-550) 301-827-2090 , Project Manager  
S. TSO (HFD-550) 301-827-2539 , Review Chemist  
H. PATEL (HFD-550) 301-827-2507 , Team Leader

Overall Recommendation:

**ACCEPTABLE** on 23-APR-1998 by J. D AMBROGIO (HFD-324)301-827-0062

Establishment:  (b) (4)

DMF No:  
AADA No:

Profile:  (b) (4) OAI Status: NONE  
Last Milestone: OC RECOMMENDATION  
Milestone Date 23-APR-1998  
Decision: ACCEPTABLE  
Reason: BASED ON PROFILE

Responsibilities: FINISHED DOSAGE STERILIZER

**CENTER FOR DRUG EVALUATION AND  
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*APPLICATION NUMBER:*

**20-597/S005**

**MICROBIOLOGY REVIEW(S)**

**REVIEW FOR HFD-550  
OFFICE OF NEW DRUG CHEMISTRY  
MICROBIOLOGY STAFF HFD-805**

APR 22 1998

**Microbiologist's Review #1 of NDA 20-597/S-005  
April 22, 1998**

**A. 1. APPLICATION NUMBER:** 20-597/S-005

**APPLICANT:** Pharmacia & Upjohn  
Kalamazoo, MI 49001-0199

**2. PRODUCT NAMES:** Xalatan (latanoprost ophthalmic solution)

**3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:** 50 ug/ml,  
sterile ophthalmic solution.

**4. METHOD(S) OF STERILIZATION:** (b) (4)

**5. PHARMACOLOGICAL CATEGORY:** ophthalmic solution for the reduction  
of elevated intraocular pressure in patients with open-angle glaucoma and ocular  
hypertension.

**B. 1. DATE OF INITIAL SUBMISSION:** March 19, 1998

**2. AMENDMENT:** none

**3. RELATED DOCUMENTS:**

**4. ASSIGNED FOR REVIEW:** April 7, 1998

**5. DATE OF CONSULT REQUEST:**

**C. REMARKS:**

The supplement provides (b) (4)  
dropper tips and screw caps (b) (4)

(b) (4) The applicant submitted the supplement as "Changes  
Being Effected", but this was overturned by HFD-550. From the standpoint of  
product quality microbiology, this type of change would have only a moderate  
potential to adversely affect product identity, strength, quality, purity and potency as  
they relate to safety and effectiveness. The supplement should therefore qualify as a  
CBE.

**D. CONCLUSIONS:**

The (b) (4) The submission is recommended for approval on the basis of sterility assurance.

---

*Brenda Uratani* 4/22/98  
**Brenda Uratani, Ph.D.**  
**Review Microbiologist**

*Pat* 4/22/98

cc:

**NDA 20-597/S-005**  
**HFD-550/ Div. File**  
**HFD-805/ Uratani**  
**HFD-550/CSO/ Gorski**  
**HFD-550/H. Patel**  
**HFD-550/ S. Tso**  
**drafted by: Brenda Uratani, 4/22/98**  
**R/D initialed by P. Cooney, 4/22/98**

2 Page(s) have been Withheld in Full as b4 (CCI/TS) immediately following this page.

**CENTER FOR DRUG EVALUATION AND  
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*APPLICATION NUMBER:*

**20-597/S005**

**ADMINISTRATIVE and CORRESPONDENCE  
DOCUMENTS**



NDA 20-597/S-005

MAR 30 1998

Pharmacia & Upjohn  
Attention: Daniel G. Mannix, Ph.D.  
Director, Regulatory Affairs  
7000 Portage Road  
Kalamazoo, Michigan 49001

Dear Dr. Mannix:

We acknowledge receipt of your supplemental application for the following:

Name of Drug Product: Xalatan™ (latanoprost ophthalmic solution) Sterile Ophthalmic Solution

NDA Number: NDA 20-597

Supplement Number: S-005

Therapeutic Classification: Standard

Date of Supplement: March 19, 1998

Date of Receipt: March 20, 1998

This supplement, submitted as "Special Supplement - Changes Being Effected" under 21 CFR 314.70(c), provides for a change in the contract sterilizing facility of caps and tips.

Changes of the kind that you have proposed, in our opinion, are not the kind of changes permitted by regulation to be put into effect prior to approval of a supplement. An approved supplement is required for the proposed changes, therefore, the supplement is being reviewed under 21 CFR 314.70(b).

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on May 19, 1998, in accordance with 21 CFR 314.101(a).

NDA 20-597/S-005

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All communications concerning this supplemental application should be addressed as follows:

Division of Anti-Inflammatory, Analgesic, and  
Ophthalmic Drug Products, HFD-550  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Attention: DOCUMENT CONTROL ROOM  
5600 Fishers Lane  
Rockville, Maryland 20857

If you have any questions, please contact Lori Gorski, Project Manager, at (301) 827-2090.

Sincerely,

WAC 3/30/98

Wiley A. Chambers, M.D.  
Deputy Director  
Division of Anti-Inflammatory, Analgesic, and  
Ophthalmic Drug Products, HFD-550  
Office of Drug Evaluation V  
Center for Drug Evaluation and Research

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cc:

Original NDA 20-597

HFD-550/Div. Files

HFD-550/CSO/L.Gorski *Hand 3/26/98 COX 5/26/98*

DISTRICT OFFICE

HFD-92/DDM-DIAB

HFD-550/Dep Dir/Chambers

HFD-550/MO/Bull

HFD-550/Chem/Tso

HFD-550 Chem TL/Patel *Hand 3-30-98*

HFD-830/ONDC Division Director

Drafted by: lmgorski/March 26, 1998/gorski/pharma/20597s5.ack

Final:

SUPPLEMENT ACKNOWLEDGEMENT (AC)

*Hand 3/31/98*