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

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-597/S005

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-597/S-005

JUL 31 1998

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

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

cc:
NDA 20-597
HFD-550/Div. Files
HFD-550/DepDir/Chambers 7/31/98
HFD-550/TLChem/Patel
HFD-550/CSO/Rodriguez RRR 7/23/98
HFD-550/Chem/Tso 7/27/98
HFD-830/Chen
HFD-105
HFD-95
DISTRICT OFFICE

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

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-597/S005

CHEMISTRY REVIEW(S)

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

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

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

DRUG PRODUCT NAME

Proprietary:	Xalatan
Nonproprietary/USAN:	Latanoprost
Code Names/#'s:	PHXA41, XA41
Chemical Type/	1 P
Therapeutic Class:	**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: __X__ Rx _____ OTC

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

Chemical Name:

RELATED DOCUMENT:
DMF (b) (4) (b) (4)
letter of authorization dated 3/4/98

REMARKS/COMMENTS:

The NDA approved sterilization facility was [redacted] (b) (4) The firm requests to transfer the sterilization facility to [redacted] (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 [redacted] (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/~~Goraki~~ Rodriguez
HFD-550/Patel

Hasmukh B. Patel
6/26/98

Microbiologist Recommended Approval
SCT
7/27/98.

CDER Establishment Evaluation Report
for April 29, 1998

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** Org Code: **550**
Action Goal: District Goal: **16-JUL-1998**
Brand Name: **XALATAN (LATANOPROST)STERILE OPHTHALMIC**
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 RESEARCH

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 [redacted] (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

PVC 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 RESEARCH

APPLICATION NUMBER:

20-597/S005

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

20.1

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).

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

cc:
Original NDA 20-597
HFD-550/Div. Files
HFD-550/CSO/L.Gorski 3/26/98 3/26/98
DISTRICT OFFICE
HFD-92/DDM-DIAB
HFD-550/Dep Dir/Chambers
HFD-550/MO/Bull
HFD-550/Chem/Tso
HFD-550 Chem TL/Patel 3-30-98
HFD-830/ONDC Division Director

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

SUPPLEMENT ACKNOWLEDGEMENT (AC)