# CENTER FOR DRUG EVALUATION AND RESEARCH

## Approval Package for:

***APPLICATION NUMBER:***

# 20-597/S013

***Trade Name:*** Xalatan

***Generic Name:*** Latanprost

***Sponsor:*** Pharmacia and Upjohn

***Approval Date:*** 06/02/2000

# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# 20-597/S013

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## Reviews / Information Included in this NDA Review.

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***APPLICATION NUMBER:***

# 20-597/S013

# APPROVAL LETTER

DIVF. 20-597

NDA 20-597/S-013

JUN 12 2000

Pharmacia & Upjohn Company
Attention: Gregory G. Shawaryn
Regulatory Affairs Manager
7000 Portage Road
Kalamazoo, Michigan 49001

Dear Mr. Shawaryn:

Please refer to your supplemental new drug application dated December 7, 1999, received December 8, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Xalatan (latanoprost ophthalmic solution) Sterile Ophthalmic Solution, 0.005%.

This "Changes Being Effected in 30 days" supplemental new drug application provides for an alternate release and stability testing site for latanoprost.

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.

LNg 6/2/00

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

cc:
NDA 20-597
HFD-550/Div. Files
HFD-550/CSO/Puglisi
HFD-550/SCSO/Vaccari
HFD-550/Chem/Rodriguez
HFD-550/ChemTL/Ng
HFD-550/MO/Boyd
HFD-550/DepDir/Chambers
HFD-095/DDMS-IMT
HFD-830/DNDC Division Director
DISTRICT OFFICE

Drafted by: mjp/June 2, 2000

Initialed by:
Puglisi, M.
Vaccari, L. 6-2-00
Rodriguez, L.
Ng, L.
Boyd, W.
Chambers, W.

filename: 20597S13.DOC

APPROVAL (AP)

# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# 20-597/S013

# CHEMISTRY REVIEW(S)

Div F.

APR 15 2000

| Chemistry Review: # 1 | 1. Division: HFD-550 | 2. NDA Number: 20-597 |
|---|---|---|
| 3. Name and Address of Applicant: Pharmacia & Upjohn Company, 7000 Portage Road, Kalamazoo, Michigan 49001 | | 4. Supplement(s): Number: SCM-013 Date(s): December 7, 2000 |
| 5. Name of Drug: Xalatan™ | | 6. Nonproprietary name: Latanoprost Ophthalmic Solution |
| 7. Supplement Provides for: An alternate release and stability testing site for latanoprost. **Changes Being Effected-30.** | | 8. Amendment(s): None |
| 9. Pharmacological Category: Treatment of elevated intra-ocular pressure for patients with ocular hypertension or open-angle glaucoma. | 10. How Dispensed: $R_x$ | 11. Related Documents: N/A |
| 12. Dosage Form: Ophthalmic Solution | 13. Potency(es): Latanoprost 0.005%(50µg/mL) | |

**14. Chemical Name and Structure:** See USAN

Latanoprost, $C_{26}H_{40}O_5$, Mol. Wt. 432.6
Isopropyl (Z)-7-[(1R, 2R, 3R, 5S)-3,5-dihydroxy-2-[(3R)-3-hydroxy-5-phenylpentyl]-cyclopentyl]-5-heptenoate
*CAS-130209-82-4.*

**15. Comments:** This CBE special supplement provides equivalency data for a change in analytical testing site for latanoprost, the active pharmaceutical ingredient in Xalatan, from the Uppsala, Sweden Pharmacia & Upjohn facility to the quality control laboratories at Pharmacia & Upjohn in Puurs, Belgium.

**16. Conclusions and Recommendations:** This CBE supplement for a change in analytical testing site meets the criteria for acceptance described in the PAC-ATLS guidance for industry. The equivalency data provided shows that the analytical facility in Puurs can precisely and accurately replicate the results of the reference laboratory in Uppsala. From the CMC perspective this supplement is recommended for **approval**, contingent upon satisfactory outcome of the on-going facility inspection by the OC.

Acceptable OC recommendation was made June 2, 2000

| 17. Name: | Signature: | Date: |
|---|---|---|
| **Libaniel Rodriguez/Review Chemist** | Libaniel Rodriguez | 4-5-00 |
| **18. Concurrence:** | **Signature:** | **Date:** |
| **Linda Ng/Chemistry Team Leader** | Ng | 4/5/00 |

cc: NDA 20-597
HFD-550/Division File
HFD-550/Team Leader/L. Ng
HFD-550/CSO ~~R. Rodriguez~~ Puglisi
HFD-550/Chemist/L. Rodriguez
HFD-550/DDD/W. Chambers
HFD-830/C-W. Chen

**Chemistry Review Comments:** This CBE special Supplement provides equivalency data for a change in analytical testing site for latanoprost, the API in Xalatan, from the Uppsala, Sweden Pharmacia & Upjohn facility to the quality control laboratories at Pharmacia & Upjohn in Puurs, Belgium. The tests for drug substance release and stability include: (b) (4) (b) (4) (b) (4) methods used are unchanged and are the same as the methods approved in the original NDA.

The comparison study for four of the tests named above were performed utilizing five results from lots: 9805002, 9806003 and 9811004 of latanoprost. Each lot was tested three times on two days in each of the laboratories to obtain the five replicates. The Pharmacia & Upjhon facility in Uppsala, Sweeden was the reference laboratory. Statistical analysis of the data provided for assays of latanoprost, impurities and residual solvent measurements indicate that no practical or statistical difference in variance or mean values exist between reference and affiliate laboratories.

This CBE supplement for a change in analytical testing site meets the criteria for acceptance described in the PAC-ATLS guidance for industry. The equivalency data provided shows that the analytical facility in Puurs can precisely and accurately replicate the results of the reference laboratory in Uppsala. From the CMC perspective this supplement is recommended for **approval**, contingent upon satisfactory outcome of the on-going facility inspection by the OC.