CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

20-688 / S-001

Trade Name: Patanol

Generic Name: olopatadine

Sponsor: Alcon Laboratories

Approval Date: January 15, 1998

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-688 / S-001

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-688 / S-001

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-270/S-019
NDA 19-387/S-006
NDA 19-992/S-007
NDA 20-258/S-005
NDA 20-688/S-001
NDA 50-541/S-009

JAN 15 1998

Alcon Laboratories
Attention: Susan H. Caballa
Associate Director, Regulatory Affairs
6201 South Freeway
Fort Worth, Texas 76134-2099

Dear Ms. Caballa:

Please refer to your July 3, 1997, supplemental new drug applications submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for:

NDA Number	Supplement Number	Drug Name
19-270	S-019	BETOPTIC® (betaxolol HCl ophthalmic solution), 0.5% Ophthalmic Solution
19-387	S-006	PROFENAL® (suprofen ophthalmic solution), 1% Ophthalmic Solution
19-992	S-007	CILOXAN® (ciprofloxacin HCl ophthalmic solution), 0.3% Ophthalmic Solution
20-258	S-005	IOPIDINE® (apraclonidine HCl ophthalmic solution) 0.5% Ophthalmic Solution
20-688	S-001	PATANOL™ (olopatadine HCl ophthalmic solution) 0.1% Ophthalmic Solution
50-541	S-009	TOBREX® (tobramycin ophthalmic solution), 0.3% Ophthalmic Solution

We acknowledge receipt of your amendment dated January 8, 1998. These supplemental applications provide for an alternate manufacturing facility.

We have completed the reviews of these supplemental applications and they are approved effective as of the date of this letter.

These approvals affect only the changes specifically submitted in these supplemental applications. 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 Lori Gorski, Project Manager, at (301) 827-2090.

Sincerely,

WAC 1/15/98

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

cc: NDA 19-270
NDA 19-387
NDA 19-992
NDA 20-258
NDA 20-688
NDA 50-541
HFD-550/Div. Files
HFD-550/CSO/Gorski
HFD-550/DepDir/Chambers
HFD-550/Clin Rev/Holmes
HFD-550/Chem/Fenselau
HFD-805/Micro/Stinavage
HFD-550/Chem TL/ Patel
HFD-92
DISTRICT OFFICE
HFD-830/DNDC III

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APPROVAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-688 / S-001

APPROVABLE LETTER

9.1

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

JAN 7 1998

NDA 19-270/S-019
NDA 19-387/S-006
NDA 19-992/S-007
NDA 20-258/S-005
NDA 20-688/S-001
NDA 50-541/S-009

Alcon Laboratories
Attention: Susan H. Caballa
Associate Director, Regulatory Affairs
6201 South Freeway
Fort Worth, Texas 76134-2099

Dear Ms. Caballa:

Please refer to your July 3, 1997, supplemental new drug applications submitted under the Federal Food, Drug, and Cosmetic Act for:

NDA Number	Supplement Number	Drug Name
19-270	S-019	BETOPTIC® (betaxolol HCl ophthalmic solution), 0.5% Ophthalmic Solution
19-387	S-006	PROFENAL® (suprofen ophthalmic solution), 1% Ophthalmic Solution
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20-258	S-005	IOPIDINE® (apraclonidine HCl ophthalmic solution) 0.5% Ophthalmic Solution
20-688	S-001	PATANOL™ (olopatadine HCl ophthalmic solution) 0.1% Ophthalmic Solution
50-541	S-009	TOBREX® (tobramycin ophthalmic solution), 0.3% Ophthalmic Solution

These supplemental applications provide for an alternate manufacturing facility.

We have completed the review of these supplemental applications and they are approvable. Before these supplements may be approved, however, it will be necessary for you to provide the following information:

[ ]

Within 10 days after the date of this letter, you are required to amend the supplemental applications, notify us of your intent to amend the supplemental applications, or follow one of the other options under 21 CFR 314.110. In the absence of such action FDA may take action to withdraw the applications.

Under 21 CFR 314.102(d) of the new drug regulations, you may request an informal or telephone conference with the Division to discuss what further steps need to be taken before the applications may be approved.

These changes may not be implemented until you have been notified in writing that these supplemental applications are approved.

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

Sincerely,

WAC 1/7/98

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:
NDA 19-270
NDA 19-387
NDA 19-992
NDA 20-258
NDA 20-688
NDA 50-541
HFD-550/Div. Files
HFD-550/CSO/Gorski
HFD-550/Acting SCSO/Koerner
HFD-550/DepDir/Chambers
HFD-550/Clin Rev/Holmes
HFD-550/Chem/Yaciw
HFD-550/Chem/Fenselau
HFD-160/Micro/Stinavage
HFD-550/Chem TL/ Patel
HFD-92
DISTRICT OFFICE
HFD-830/DNDC III

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APPROVABLE (AE)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

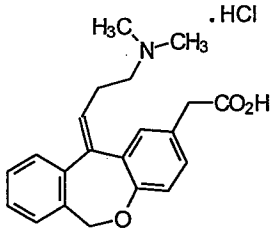
20-688 / S-001

CHEMISTRY REVIEW(S)

DEC 2 2 1997

Chemistry Review Review #1	1. Division HFD-550	2. NDA Number #20-688
3. Name and Address of Applicant Alcon Laboratories, Inc. 6201 South Freeway Fort Worth, TX 76134		4. Supplement Number Date SCM-001 03-JUL-97
5. Name of Drug PATANOL 0.1%	6. Nonproprietary Name Olopatadine Hydrochloride	
7. Supplement Provides for: Alternate manufacturing site [redacted]		8. Amendment(s)
9. Pharmacological Category Short-term prevention of itching of eye due to allergic conjunctivitis	10. How Dispensed Rx	11. Related Documents NDA #19-387 (SCM-006) NDA #19-992 (SCM-007) NDA #19-270 (SCM-019) NDA #20-258 (SCM-005) NDA #50-541 (SCM-009) NDA #20-226 (SCM-008)
12. Dosage Form Ophthalmic solution	13. Potency(ies): Olopatadine hydrochloride 0.111% (equivalent to 0.1% olopatadine base)	

14. Chemical Name and Structure see USAN



$C_{21}H_{24}ClNO_3$

Mol.Wt.: 373.88

(Z)-11-[3-(Dimethylamino)propylidene]-6,11-dihydrodibenz[b,e]exepine-2-acetic acid hydrochloride

OLOPATIDINE HCl

[redacted]

[redacted]

17. Name Allan Fenselau	**Signature**	Allan Fenselau	**Date** 12/19/97
Concurrence Hasmukh B. Patel	**Signature**	for HP	**Date** 12/22/97

cc: **NDA #20-688**
HFD-550/Division File
HFD-550/CSO/L.Gorski
HFD-550/CHEM/A.Fenselau
HFD-550/CHEM/TeamLdr/H.Patel
HFD-550/MO/J.Bull
HFD-550/SMO/W.Chambers
Doc ID: n20688s.001

9 Page(s) Withheld

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_____ Draft Labeling

_____ Deliberative Process

Withheld Track Number: Chemistry- 1a

10-C

JAN 7 1998

AMENDMENT TO CMC REVIEWS FOR

NDA 19-270/S-019 (BETOPTIC 0.5% Ophthalmic Solution)
NDA 19-387/S-006 (PROFENAL 1% Ophthalmic Solution)
NDA 19-992/S-007 (CILOXAN 0.3% Ophthalmic Solution)
NDA 20-258/S-005 (IOPIDINE 0.5% Ophthalmic Solution)
NDA 20-688/S-001 (PATANOL 0.1% Ophthalmic Solution)
NDA 50-541/S-009 (TOBREX 0.3% Ophthalmic Solution)

The original Microbiology Review [MR] of the supplement recommended approval on the basis of sterility assurance (see attached MR by P. Stinavage dated 23-OCT-97). However, in a Microbiology Review Amendment dated 19-NOV-97 (also attached) concern was expressed for the [redacted] Qualitative terms used in the review, such as " [redacted] were finally quantified. In the case of the present submission, the indicated [redacted] both parameters substantially exceed the [redacted] which have been approved for the present manufacturing site(s). Subsequent discussion between members of the Microbiology Review team and the sponsor permitted approval by the MR team (see attached Microbiology Review Amendment 2 dated 07-JAN-98). The sponsor has **FAXED** to the Microbiology Review team an agreement to [redacted] which are presently approved for these products at their existing manufacturing site(s), and hard copy is to follow (see attached copy of an Alcon fax dated 05-JAN-98). The point emphasized by MR is that Agency inspection of the facility has revealed that the recorded [redacted] The use of these [redacted]

Consequently, the recommendation is that this request to manufacture the six ophthalmic products at the alternative [redacted] may be approved.

Allan Fenselau 1/7/98
Allan Fenselau — Date
Chemistry Reviewer — HFD-550

Hasmukh B. Patel 1/7/98
Hasmukh B. Patel — Date
Team Leader — HFD-550

Chi-wan Chen 1/7/98
Chi-wan Chen — Date
Director DNDCIII — HFD-830

NDA 19-270
NDA 19-387
NDA 19-992
NDA 20-258
NDA 20-688
NDA 50-541
HFD-550/Fenselau
HFD-550/Yaciw
HFD-550/Chambers
HFD-550/Gorski
HFD-550/Div Files

101

JAN 5 1998

NDA #20-688
SCM-001

AMENDMENT to REVIEW
PATANOL™ 0.1% Ophthalmic Solution

Alcon Laboratories, Inc.

MICROBIOLOGY REVIEW

APPROVABLE

The original Microbiology Review [MR] of the supplement recommended approval on the basis of sterility assurance (see attached MR by P. Stinavage dated 23-OCT-97). However, in a Microbiology Review Amendment dated 19-NOV-97 (also attached) concern was expressed for the [redacted] Qualitative terms used in the review, such as [redacted] have finally been quantified. In the case of the present submission, the indicated [redacted] substantially exceed the [redacted] which have been approved for the present manufacturing site(s). Based on this information, the opinion of the Chemistry Review is that the issues raised from the Microbiology Review Amendment (dated 19-NOV-97) need to be fully resolved by official receipt of their agreement to the [redacted] pproved for this product at their existing manufacturing site(s) and by receipt of the details of actions to be taken if the [redacted] Consequently, the recommendation is that this request to manufacture PATANOL™ 0.1% Ophthalmic Solution at the alternative [redacted] considered Approvable only.

Allan Fenselau 1/5/98

Allan Fenselau
Chemistry Reviewer

Date
HFD-550

Concur for HP 1/5/98

Hasmukh B. Patel
Team Leader

Date
HFD-550

NDA 20-688
HFD-550 - Div Files
HFD550 - Chambers
HFD-550 Gorski
HFD-550 Fenselau
HFD-550 - Yaciw

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-688 / S-001

MICROBIOLOGY REVIEW(S)

9.1

OCT 23 1997

REVIEW FOR HFD-550
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW OF SUPPLEMENT
21 October 1997

A. 1. NDA 19-270/S-019 NDA 19-387/S-006
NDA 19-992/S-007 NDA 20-258/S-005
NDA 20-688/S-001 NDA 50-541/S-003

APPLICANT: Alcon Laboratories, Inc.
6201 South Freeway
Fort Worth, TX 76134-2099

2. PRODUCT NAME:

NDA 19-270:	Betoptic® (betaxolol HCl) 0.5% Ophthalmic Solution
NDA 19-387:	Profenal® (suprofen) 1% Ophthalmic Solution
NDA 19-992:	Ciloxan® (ciprofloxacin HCl) 0.3% Ophthalmic Solution
NDA 20-258:	Iopidine® (apraclonidine HCl) 0.5% Ophthalmic Solution
NDA 20-688:	Patanol® (olopatadine HCl) 0.1% Ophthalmic Solution
NDA 50-541:	Tobrex® (tobramycin) 0.3% Ophthalmic Solution

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:
The products are ophthalmic solutions for instillation into the eye.

4. METHODS OF STERILIZATION:
The products are

5. PHARMACOLOGICAL CATEGORY and/or PRINCIPLE INDICATION:
The products have a variety of indications for treatment of conditions affecting the eye.

B. 1. DATE OF INITIAL SUBMISSION: 3 July 1997

2. DATE OF AMENDMENT: (none)

3. RELATED DOCUMENTS: Original NDA's 19-270, 19-387, 19-992, 20-

4. ASSIGNED FOR REVIEW: 28 July 1997

C. REMARKS: These submissions have been submitted as a bundled supplement to seek approval for an alternate manufacturing site

[ ]

[ ]

D. CONCLUSIONS: The applications are recommended for approval on the basis of sterility assurance.

23 October 1997

Paul Stinavage, Ph.D.

PMC 10/23/97

cc: Original NDA 19-270
NDA 19-992
NDA 20-688
NDA 19-387
NDA 20-258
NDA 50-541
HFD-550/D.A. Gunter
HFD-805/Consult File/Stinavage

Drafted by: P. Stinavage, 21 October 1997
R/D initialed by P. Cooney

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_____ Deliberative Process

Withheld Track Number: Microbiology- 1a