CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

050616sOrig1s015

Trade Name:	**TobraDex, Ophthalmic Ointment**
Generic or Proper Name:	(Tobramycin and Dexamethasone)
Sponsor:	**Novartis**
Approval Date:	September 28, 1999
Indication:	TOBRADEX Ophthalmic Ointment is indicated for steroid-responsive inflammatory ocular conditions for which a corticosteroid is indicated and where superficial bacteria ocular infection or a risk of bacterial ocular infection exists.

CENTER FOR DRUG EVALUATION AND RESEARCH

050616sOrig1s015

CONTENTS

Reviews / Information Included in this NDA Review.

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Cross Discipline Team Leader Review	
Clinical Review(s)	
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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

050616sOrig1s015

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-369/S-003
NDA 50-344/S-018
NDA 50-555/S-016
NDA 50-616/S-015

SEP 28 1999

Alcon Laboratories, Inc.
Attention: Sarah J. Cantrell
Manager, Regulatory Affairs
6201 South Freeway
Fort Worth, TX 76134-2099

Dear Ms. Cantrell:

Please refer to your supplemental new drug applications dated June 22, 1999, received June 23, 1999, submitted under the Federal Food, Drug, and Cosmetic Act for the following:

NDA 20-369/S-003	Ciloxan (ciprofloxacin HCl ophthalmic ointment), 0.3% as base
NDA 50-344/S-018	Statrol (neomycin and polymyxin B sulfates ophthalmic ointment, USP)
NDA 50-555/S-016	Tobrex (tobramycin ophthalmic ointment), 0.3% Ophthalmic Ointment
NDA 50-616/S-015	Tobradex (tobramycin and dexamethasone ophthalmic ointment)

These supplemental new drug applications provide for a change in the ointment tube used in the media fill validation.

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

These approvals affect only the change 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, contact Raphael R. Rodriguez, Project Manager, at (301) 827-2090.

Sincerely,

LN 9/28/99

Linda L. Ng, Ph.D.
Chemistry Team Leader, DNDC III 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

cc:
NDA 20-369
NDA 50-344
NDA 50-555
NDA 50-616
HFD-550/Div. Files (copy for each NDA)
HFD-550/DepDir/Chambers VMAC 9/27/99
HFD-550/MO/Boyd LNg 9/22/99
HFD-550/TLChem/Ng
HFD-550/Chem/RodriguezL. 9/22/99 L.R. 9-22-99
HFD-550/PM/RodriguezR 9/22/99
HFD-550/PM/Gorski
HFD-095/DDMS-IMT
HFD-830/DNDC Division Director
DISTRICT OFFICE

Drafted by: rrr/September 22, 1999
Initialed by:
final:
filename: 20369S3

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

050616sOrig1s015

PRODUCT QUALITY REVIEW(S)

SEP 15 1999

Chemistry Review # 1	1. Division: HFD-550	2. NDA Number: 50616

3. Name and Address of Applicant:
~~Falcon Pharmaceuticals, LTD~~. Alcon Lab
6201 south Freeway R7-18
Fort Worth, Texas 76134- 2099

4. Supplement(s):
Number: SCP - 015
Date(s): June 22, 1999

5. Name of Drug:
Tobradex®

6. Nonproprietary name:
Tobramycin and dexamethasone

7. Supplement Provides for:
Change in the ointment tube used in the media fill validation.

8. Amendment(s):

9. Pharmacological Category:
Antiinflamatory, Antibiotic.

10. How Dispensed:
℞

11. Related Documents:
NDA # 20-369/SCP - 003
NDA # 50-065/SCP - 037 – Falcon Pharmaceuticals
NDA # 50-555/SCP - 016
NDA # 50-344/SCP - 018
AADA # 61-648
ANDA # 80-021
ANDA # 87-771

12. Dosage Form:
Ophthalmic Ointment

13. Potency(ies): Tobramycin 0.3%, dexamethasone 0.1%.

14. Chemical Name and Structure: See USAN
Tobramycin, *O*-3-Amino-3-deoxy-α-D-glucopyranosyl-(1→4)-*O*-[2,6-diamino-2,3,6-trideoxy-α-D-ribohexopyranosyl-(1→6)]-2-deoxy-L-streptamine. $C_{18}H_{37}N_5O_9$, Mol. Wt. 467.52.

Dexamethasone, 9-Fluoro-11β,17,21-trihydroxy-16α-methylpregna-1,4-diene-3,20dione. $C_{22}H_{29}FO_5$. Mol. Wt 392.47

15. Comments: This supplement is for a change in the ointment tube used in the [redacted] (b) (4). The change is from a [redacted] since the supplier of the [redacted] (b) (4) will no longer be producing this item. The [redacted] (b) (4) tubes were tested for compatibility with the media fill for the [redacted] (b) (4)

16. Conclusions and Recommendations: [redacted] (b) (4) (b) (4) (b) (4). For these reasons the change to [redacted] (b) (4) tubes for the [redacted] (b) (4) is **Approved.**

17. Name:	Signature:	Date:
Libaniel Rodriguez, Review Chemist	Libaniel Rodriguez	9-15-99
18. Concurrence:	**Signature:**	**Date:**
Linda Ng, Team Leader	Linda Ng	9/15/99

cc: NDA 20-191
HFD-550/Division File
HFD-550/Team Leader/L. Ng
HFD-550/CSO/R.Rodriguez
HFD-550/Chemist/L. Rodriguez
HFD-550/DDD/W. Chambers
HFD-830/DD/CW. Chen

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

050616sOrig1s015

CLINICAL MICROBIOLOGY/VIROLOGY REVIEW(S)

REVIEW TO HFD-550
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY TEAM
MICROBIOLOGIST REVIEW OF SUPPLEMENTS
6 AUGUST 1999

AUG. 27 1999

A. NDA and Drug Products:

NDA 20-369/S-003 CILOXAN (ciprofloxacin HCl ophthalmic ointment) 0.3% as base
NDA 50-334/S-018 STATROL Neomycin and Polymyxin B Sulfates Ophthalmic Ointment, USP
NDA 50-616/S-015 TOBRADEX (tobramycin and dexamethasone ophthalmic ointment)
NDA 50-555/S-016 TOBREX (tobramycin 0.3%) Ophthalmic Ointment

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

DOSAGE FORM: Topical ointments for ophthalmic use
METHOD OF STERILIZATION: Aseptic processing

[redacted] (b) (4)

B. INITIAL APPLICATION DATE: 22 June 1999
DATE RECEIVED: 28 June 1999
ASSIGNED FOR REVIEW: 29 June 1999

C. REMARKS: The supplements listed provide for a change in the tubes used during media fill validation runs.

D. CONCLUSIONS: The NDA supplements 20-369/S-003, 50-334/S-018, 50-616/S-015 and 50-555/S-016 which provide for a change in ointment tubes used during media fill validation runs are recommended for approval from the standpoint of product quality microbiology. The applicant may use [redacted] (b) (4) tubes, [redacted] (b) (4) [redacted] (b) (4) from the supplier [redacted] (b) (4) in the [redacted] (b) (4). Please see section E for Review Notes.

6 Aug 99

Patricia F. Hughes, Ph. D.
Review Microbiologist

Cc.: Original NDA20-369
NDA 50-334
NDA 50-616
NDA 50-555
HFD-160 /Consult File
HFD-805/PFHughes
HFD-550/R.Rodriguez/L.Ng/L.Gorski
HFD-550/Division File
Drafted by PFHughes/10 May 1999
R/D Initialed by PHCooney

D. Thomas for PHC
8-27-99

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L. Ng.
→ Li

AUG. 27 1999

REVIEW TO HFD-550
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY TEAM
MICROBIOLOGIST REVIEW OF SUPPLEMENTS
6 AUGUST 1999

A. NDA and Drug Products:

NDA 20-369/S-003 CILOXAN (ciprofloxacin HCl ophthalmic ointment) 0.3% as base
50249 NDA (b) (4) /S-018 STATROL Neomycin and Polymyxin B Sulfates Ophthalmic Ointment, USP
NDA 50-616/S-015 TOBRADEX (tobramycin and dexamethasone ophthalmic ointment)
NDA 50-555/S-016 TOBREX (tobramycin 0.3%) Ophthalmic Ointment

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

DOSAGE FORM: Topical ointments for ophthalmic use
METHOD OF STERILIZATION: Aseptic processing

(b) (4)

B. INITIAL APPLICATION DATE: 22 June 1999
DATE RECEIVED: 28 June 1999
ASSIGNED FOR REVIEW: 29 June 1999

C. REMARKS: The supplements listed provide for a change in the tubes used during (b) (4).

D. CONCLUSIONS: The NDA supplements 20-369/S-003, 50-334/S-018, 50-616/S-015 and 50-555/S-016 which provide for a change in ointment tubes used during media fill validation runs are recommended for approval from the standpoint of product quality microbiology. The applicant may use (b) (4) tubes, (b) (4) (b) (4) from the supplier (b) (4) (b) (4). Please see section E for Review Notes.

6 Aug 99
Patricia F. Hughes, Ph. D.
Review Microbiologist

Cc.: Original NDA20-369
NDA 50-334
NDA 50-616
NDA 50-555
HFD-160 /Consult File
HFD-805/PFHughes
HFD-550/R.Rodriguez/L.Ng/L.Gorski
HFD-550/Division File
Drafted by PFHughes/10 May 1999
R/D Initialed by PHCooney

D. Thomas for PHC
8-27-99

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~~R. Uppoore~~
Should go to A Rodriguez
WF 8/10/99

JUL 20 1999

REVIEW FOR HFD-550
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW OF SUPPLEMENT
16 July 1999

A. 1. NDA 50-065/SCP-037
APPLICANT: Falcon Pharmaceuticals, Ltd.
Alcon Laboratories, Inc.
6201 South Freeway
Fort Worth, TX 76134-2099

344
NDA 20-369/S-003 NDA 50-~~334~~/S-018 NDA 50-616/S-015
NDA 50-555/S-016
APPLICANT: Alcon Laboratories
6201 South Freeway
Fort Worth, TX 76134-2099

2. PRODUCT NAMES: MAXITROL® (neomycin and polymyxin B sulfates and dexamethasone ophthalmic ointment), CILOXAN® Ointment, STATROL® Ointment, TOBRADEX® Ointment, TOBREX® Ointment

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

4. METHODS OF STERILIZATION:
The products are aseptically filled.

5. PHARMACOLOGICAL CATEGORY and/or PRINCIPLE INDICATION:
(b) (4)

B. 1. DATE OF INITIAL SUBMISSION: 22 June 1999

2. DATE OF AMENDMENT: (none)

3. RELATED DOCUMENTS: ANDA's 80-021, 87-771
AADA 61-648

4. ASSIGNED FOR REVIEW: 6 July 1999

C. (b) (4) [redacted]

D. CONCLUSIONS: The supplement is recommended for approval from the standpoint of microbiology.

16 July 1999
Paul Stinavage, Ph.D.
7/20/99

cc: Original NDA 50-065, NDA 20-369, NDA 50-334, NDA 50-616, NDA 50-555
HFD-550/L. Ng/A. Fenselau/R. Rodriguez/R. Uppoor
HFD-600/A. High/M. Fanning
HFD-805/Consult File/Stinavage

Drafted by: P. Stinavage, 16 July 1999
R/D initialed by P. Cooney

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

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ADMINISTRATIVE AND CORRESPONDENCE DOCUMENTS

13.1

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 50-616/S-015

Alcon Laboratories, Inc.
6201 South Freeway
Fort Worth, Texas 76134

JUL 8 1999

Attention: Sarah J. Cantrell
Manager, Regulatory Affairs

Dear Ms. Cantrell:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: Tobradex® (tobramycin and dexamethasone) Ophthalmic Ointment

NDA Number: 50-616

Supplement Number: S-015

Date of Supplement: June 22, 1999

Date of Receipt: June 23, 1999

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on August 22, 1999 in accordance with 21 CFR 314.101(a).

All communications concerning this NDA should be addressed as follows:

Food and Drug Administration
Division of Anti-Inflammatory, Analgesic and
Ophthalmic Drug Products, HFD-550
Office of Drug Evaluation V
Center for Drug Evaluation and Research
Attention: Document Control Room
5600 Fishers Lane
Rockville, MD 20857

Sincerely,

6/29/99

FOR Anthony M. Zeccola
Chief, Project Management Staff
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 50-616/S-015
HFD-550/Div. Files
HFD-550/CSO/R. Rodriguez

SUPPLEMENT ACKNOWLEDGEMENT