

# 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

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

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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.

NDA 20-369/S-003  
NDA 50-344/S-018  
NDA 50-555/S-016  
NDA 50-616/S-015  
Page 2

If you have any questions, contact Raphael R. Rodriguez, Project Manager, at (301) 827-2090.

Sincerely,

*LNf* 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 *WAC 9/22/99*  
HFD-550/MO/Boyd *8/29 9/22/99*  
HFD-550/TLChem/Ng  
HFD-550/Chem/RodriguezL. *9/22/99 L.R. 9-22-99*  
HFD-550/PM/RodriguezR *MM 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)

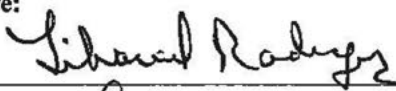
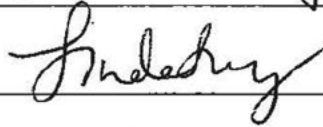
**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**050616sOrig1s015**

**PRODUCT QUALITY REVIEW(S)**

SEP 15 1999

|                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                           |                                                                                                                                                                                                                    |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Chemistry Review</b><br># 1                                                                                                                                                                                                                                                                                                                                                                                                           | <b>1. Division:</b><br>HFD-550                                                                            | <b>2. NDA Number:</b><br>50616                                                                                                                                                                                     |
| <b>3. Name and Address of Applicant:</b><br>Falcon Pharmaceuticals, LTD. Alcon Lab<br>6201 south Freeway R7-18<br>Fort Worth, Texas 76134- 2099                                                                                                                                                                                                                                                                                          |                                                                                                           | <b>4. Supplement(s):</b><br>Number: SCP - 015<br>Date(s): June 22, 1999                                                                                                                                            |
| <b>5. Name of Drug:</b><br>Tobradex®                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                           | <b>6. Nonproprietary name:</b><br>Tobramycin and dexamethasone                                                                                                                                                     |
| <b>7. Supplement Provides for:</b><br>Change in the ointment tube used in the media fill validation.                                                                                                                                                                                                                                                                                                                                     |                                                                                                           | <b>8. Amendment(s):</b>                                                                                                                                                                                            |
| <b>9. Pharmacological Category:</b><br>Antiinflammatory, Antibiotic.                                                                                                                                                                                                                                                                                                                                                                     | <b>10. How Dispensed:</b><br>Rx                                                                           | <b>11. Related Documents:</b><br>NDA # 20-369/SCP - 003<br>NDA # 50-065/SCP - 037 -- Falcon Pharmaceuticals<br>NDA # 50-555/SCP - 016<br>NDA # 50-344/SCP - 018<br>AADA # 61-648<br>ANDA # 80-021<br>ANDA # 87-771 |
| <b>12. Dosage Form:</b><br>Ophthalmic Ointment                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                           |                                                                                                                                                                                                                    |
| <b>13. Potency(ies):</b> Tobramycin 0.3%, dexamethasone 0.1%.                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                           |                                                                                                                                                                                                                    |
| <b>14. Chemical Name and Structure:</b> See USAN<br>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 <sub>18</sub> H <sub>37</sub> N <sub>5</sub> O <sub>9</sub> , Mol. Wt. 467.52.<br><br>Dexamethasone, 9-Fluoro-11β,17,21-trihydroxy-16α-methylpregna-1,4-diene-3,20dione. C <sub>22</sub> H <sub>29</sub> FO <sub>5</sub> . Mol. Wt 392.47 |                                                                                                           |                                                                                                                                                                                                                    |
| <b>15. Comments:</b> This supplement is for a change in the ointment tube used in the (b) (4). The change is from a (b) (4) since the supplier of the (b) (4) will no longer be producing this item. The (b) (4) tubes were tested for compatibility with the media fill for the (b) (4)                                                                                                                                                 |                                                                                                           |                                                                                                                                                                                                                    |
| <b>16. Conclusions and Recommendations:</b> (b) (4)<br>(b) (4) tubes for the (b) (4) is Approved. (b) (4). For these reasons the change to (b) (4)                                                                                                                                                                                                                                                                                       |                                                                                                           |                                                                                                                                                                                                                    |
| <b>17. Name:</b><br>Libaniel Rodriguez, Review Chemist                                                                                                                                                                                                                                                                                                                                                                                   | <b>Signature:</b><br> | <b>Date:</b><br>9-15-99                                                                                                                                                                                            |
| <b>18. Concurrence:</b><br>Linda Ng, Team Leader                                                                                                                                                                                                                                                                                                                                                                                         | <b>Signature:</b><br> | <b>Date:</b><br>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

(b) (4)

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

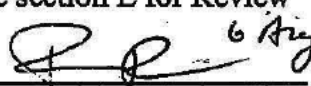
C. REMARKS: The supplements listed provide for a change in the tubes used during media fill validation runs.

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 (b) (4) tubes, (b) (4)

(b) (4) from the supplier (b) (4)

(b) (4) in the (b) (4). Please see section E for Review

Notes.

  
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. Hughes for PHC*  
*8-21-99*

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CCI) Immediately Following this Page

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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:

50749 NDA 20-369/S-003 CILOXAN (ciprofloxacin HCl ophthalmic ointment) 0.3% as base  
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) 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. Hughes for PHC*  
8 - 21 - 99

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

should go to Rodriguez

8/10/99

JUL 20 1999

A. 1. NDA 50-065/SCP-037

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

NDA 20-369/S-003    NDA 50-<sup>344</sup>~~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)

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

  
Paul Stinavage, Ph.D. 16 July 1999  
PWC 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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*APPLICATION NUMBER:*

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**ADMINISTRATIVE AND CORRESPONDENCE**  
**DOCUMENTS**





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,

FOR *MM* 6/29/99  
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

NDA 50-616/S-015

Page 2

cc:

Original NDA 50-616/S-015

HFD-550/Div. Files

HFD-550/CSO/R. Rodriguez

SUPPLEMENT ACKNOWLEDGEMENT