

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number **20-369**

CHEMISTRY REVIEW(S)

DEC 23 1993

DIVISION OF ANTI-INFECTIVE DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA #: 20-369 **CHEM.REVIEW #:** 01 **REVIEW DATE:** 09-01-93

SUBMISSION/TYPE **DOCUMENT DATE** **CDER DATE** **ASSIGNED DATE**

ORIGINAL 05-21-93 05-26-93 07-10-93

NAME & ADDRESS OF APPLICANT: Alcon Laboratories, Inc.
6201 South Freeway
Ft. Worth, Texas 76134

DRUG PRODUCT NAME

Proprietary: Ciloxin Ophthalmic Ointment, 0.3%
Nonproprietary: ciprofloxacin HCl Ophth. Ointment
Code Names/#'s:

ANDA Suitability Petition/DESI/Patent Status:

N/A

PHARMACOLOGICAL CATEGORY/INDICATION: Quinolone

DOSAGE FORM:

Ointment

STRENGTHS:

0.3%

ROUTE OF ADMINISTRATION:

Ocular

DISPENSED:

XXXXX Rx _____ OTC

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

- (a) 1-Cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinolinecarboxylic acid monohydrochloride monohydrate
- (b) 3-Quinolonecarboxylic acid, 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl), monohydrochloride, monohydrate

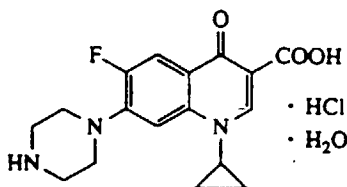
Other Code Names: ALØ25Ø7A, Bay o 9867 (HCl salt)

CAS Registry Number: 86393-32-0

Molecular Formula: C₁₇H₁₈FN₃O₃•HCl•H₂O

Molecular Weight: 385.82

Structural Formula



NDA 20-369
ALCON LABS
CILOXAN

SUPPORTING DOCUMENTS:

Reference to NDAs and DMFs have been submitted; see Appendix 1.

REMARKS/COMMENTS:

Ciprofloxacin Hydrochloride is the active ingredient in Ciprofloxacin Ointment. It is the same active ingredient in Ciprofloxacin Ophthalmic Solution (Alcon's approved NDA 19-992). Ciprofloxacin HCl is a USP compendial item (USPXXII, third supplement, page 2324).

CONCLUSIONS & RECOMMENDATIONS:

The application is not approvable for manufacturing and controls under Section 505 of the Act. Specific items which are not approvable are identified under the following headings: container/closure, stability, manufacturing, Environment Assessment, Method Validation and Establishment Inspection.

10/5/93

B. V. Shetty, Ph.D.
Senior Expert Chemist

cc: Orig. NDA 20-369
HFD-520/Division File
HFD-520/BVShetty/td/10/4/93
HFD-520/MO/WC/TC
HFD-520/Pharm/Osterberg
HFD-520/Micro/Sheldon
HFD-520/CSO/Fogarty
HFD-102/CKumkumian [#1 only]
R/D Init by: SUPVCHEM/WHDeCamp
filename: N20369.rv1

10/9/93
12/22/93

DIVISION OF ANTI-INFECTIVE DRUG PRODUCTS
CHEMIST'S REVIEW #2

A. 1. NDA 20-369

2. PRODUCT NAME:

Proprietary: Ciloxan Ophthalmic Ointment 0.3%

Non-proprietary: Ciprofloxacin HCl Ophthalmic
Ointment

Code Name and/or Number: MP-123456B

B. 1. INITIAL SUBMISSION: May 21, 1993

2. AMENDMENTS: August 20, 1993

C. REMARKS: In reference to the request to submit Environmental Impact Analysis report (see chemist's review dated 10/5/93), the firm has submitted the following information.

- 1) The firm states that the and sterilization of ciprofloxacin HCl powder will be carried out at Alcon Laboratories, Ft. Worth, Texas. The product will be produced at Alcon (Puerto Rico) Inc., Road 925 Barrio Junquito, Humacao, Puerto Rico 00791. The firm has submitted applicable environmental regulations (exhibit 1) and states that it will meet applicable Water Regulations/Laws/Acts Texas (as amended) for water, air. Also, it will meet Territorial Regulations/Laws/Acts (as amended) Puerto Rico for Water, Air and Solid Waste Land Use (exhibit 2).
- 2) The firm states that it will comply with all current municipal, state and federal efficient emission regulations/standards. Additionally, Alcon Laboratories, Inc., will comply with all applicable regulations/standards regarding occupational exposure.
- 3) The firm states that the approval of the NDA will not adversely affect their operations or compliance with applicable regulations with regard to introduction of substances into the environment [21 CFR 25.31a(b)(3)(i)].
- 4) The firm states that the market volume for the product is expected to be approximately

- 5) The firm states that no significant air emissions are generated from manufacturing process. The by-products are minimal and the discharge of effluent is fully within compliance of all applicable standards. As a matter of good practice, facilities conduct baseline effluent sampling to assure compliance to set standards. All wastes are disposed of within the dictates of current regulations.
- 6) Residual amounts of waste generated are minimal in nature relative to total effluent and/or solid waste. Regulatory compliance listing and controls impact for ciprofloxacin hydrochloride (exhibit 3).
- 7) The Alcon Laboratories Inc., Corporate Senior Director, Mr. Thomas O. Jones, certifies that the firm will comply with all current municipal, state and federal effluent emission regulations/standards. Additionally, the firm will comply with all applicable regulations/standards regarding occupational exposure. The statement was signed by Mr. Jones on 8/9/93.

D. **CONCLUSIONS AND/OR RECOMMENDATIONS:** The information on Environment Impact Analysis is satisfactory (chemist's review dated 10/5/93, #12).

The NDA remains
unapprovable.

4/5/94

B.Vithal Shetty, Ph.D.

cc: Orig: NDA 20-369

HFD-540

HFD-520/Buko

HFD-540/~~Shetty~~ *Carener*

HFD-541/~~Shetty~~ *joyce*

HFD-520/Shetty

init. by SUPVCHEM/SBRoy/ *WA 4/5/94*

td:4/5/94

n20369.rv2

MAY 10 1994

DIVISION OF TOPICAL DRUG PRODUCTS
CHEMIST'S REVIEW #3

A. 1. NDA 20-369 DATE COMPLETED: 12/28/93

ADDRESS: Alcon Laboratories, Inc.
6201 South Freeway
Ft. Worth, Texas 76134

2. PRODUCT NAME(S):

Proprietary: Ciloxan Ophthalmic Ointment
Non-proprietary: Ciprofloxacin HCl Ophthalmic
Ointment

Code name and/or number: MP-123456B

B. 1. Initial Submission: 5/26/93

2. Amendments: 12/21/93

C. REMARKS: SEE ATTACHED

D. CONCLUSIONS AND/OR RECOMMENDATIONS: The NDA remains not
approvable

12/28/93

B. Vithal Shetty, Ph.D.

cc: Orig. NDA 20-369/RV3

HFD-540 *92/5/12/94*

HFD-540/MO/

HFD-540/CSO/Joyce

HFD-540/CHEM/BVShetty

R/D initialed by SupvChem/WHDeCamp/*WJ 5/10/94*

N20369.rv3

td/5/10/94

*(original review lost, was given
final concurrence 4/5/94)*

11

DIVISION OF TOPICAL DRUG PRODUCTS
CHEMIST'S REVIEW #4

A. 1. NDA 20-369

DATE COMPLETED: 4/6/94

ADDRESS: Alcon Laboratories, Inc.
6201 South Freeway
Ft. Worth, Texas 76134

2. PRODUCT NAME(S):

Proprietary: Ciloxan Ophthalmic Ointment,
0.3%

Non-proprietary: ciprofloxacin HCl Ophthalmic
Ointment

Code name and/or number: MP-123456B

B. REMARKS: With regard to the stability of the drug product
(see Chemist's Review #1 dated 9/1/93), the firm on 12/21/93
has submitted acceptable explanation (see Review #3) for the
non-uniformity of the ointment.

C. CONCLUSIONS AND/OR RECOMMENDATIONS: The proposed 36 months
expiry date is acceptable.

4/9/94

B. Vithal Shetty, Ph.D.

cc: Orig. NDA 20-369

HFD-540

HFD-540/MO/

HFD-540/CSO/Joyce

HFD-540/CHEM/BVShetty

R/D initialed by SupvChem/WHDeCamp/

N20369.rv4

td/4/6/94

ND 4/11/94

HFD550/chem/uppor

Division of Anti-inflammatory, Analgesic and Ophthalmic Drugs
Review of Chemistry, Manufacturing, and Controls

NDA #: 20-369

REVIEW # 6

DATE OF REVIEW: 12-17-97

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
ORIGINAL SUBMISSION	21-May-93	24-May-93	
AMENDMENT, AZ	20-Jun-97	24-Jun-97	02-Jul-97
AMENDMENT, BI	10-Nov-97	13-Nov-97	See Micro. Review
AMENDMENT, BZ	19-Nov-97	01-Dec-97	08-Dec-97
AMENDMENT, BC	24-Nov-97	28-Nov-97	08-Dec-97
AMENDMENT, BZ	02-Dec-97	02-Dec-97	08-Dec-97

NAME & ADDRESS OF APPLICANT:

Alcon Laboratories, Inc.
6201 South Freeway, R3-14
Fort Worth, Texas 76134.

Contact: Cheryl B. Anderson, Pharm.D.
Manager, Regulatory Affairs
817-551-4325.

DRUG PRODUCT NAME

Proprietary: CILOXAN Ophthalmic Ointment, 0.3% (as ciprofloxacin).
Established: Ciprofloxacin hydrochloride ophthalmic ointment.
Code Name/#: NDC # 00065-0654-35 (From page 4-0248).
Chem.Type/Ther.Class: 3, Standard Review/Drug Class # 4041322.

PHARMACOLOGIC CATEGORY:

Broad spectrum fluoroquinolone antimicrobial ointment for topical ophthalmic application.

DOSAGE FORM: Sterile Ophthalmic Ointment.

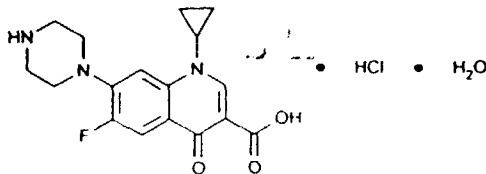
STRENGTHS: 0.3% (as ciprofloxacin base).
0.33% (as ciprofloxacin hydrochloride anhydrous).
0.35% (as ciprofloxacin hydrochloride monohydrate).

ROUTE OF ADMINISTRATION: Topical ophthalmic application.

DISPENSED: X Rx OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA AND WEIGHT:

Ciprofloxacin Hydrochloride (monohydrate).



C₁₇H₁₈FN₃O₃·HCl·H₂O 385.82
3-Quinolincarboxylic acid, 1-cyclopropyl-6-fluoro-1,4-dihydro-
4-oxo-7-(1-piperazinyl)-, monohydrochloride, monohydrate
1-Cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-
quinolincarboxylic acid, monohydrochloride, mono-
hydrate [86393-32-0].

REMARKS:

This CMC Review # 5 is in continuation to previous CMC Review # 4 dated 4/6/94 for this NDA. From the CMC standpoint, the NDA was NOT APPROVABLE

(Ref: Dr. B.V. Shetty's Chemist's Review # 3, dated 12/28/93). The information contained in this amendment replaces the sections submitted in the original application, unless otherwise noted (ref: Cover Letter). The NDA amendment was reviewed. Review details are enclosed in Chemist's Review Notes, pages 3 to 16.

CONCLUSIONS & RECOMMENDATIONS:

From the CMC standpoint, this application is recommended for a NOT APPROVABLE action based on the recommendation of the Microbiology Staff of ONDC, the details of which are provided in Attachment 8.

12/17/1997
Rajendra Upoor, Ph.D., R.Ph.
Review Chemist, HFD-550/830

HP 12/17/1997
Hasmukh Patel, Ph.D.
Chemistry Team Leader, HFD-550/830

cc:

Orig. NDA 20-369
HFD-550/Division File
HFD-550/Chem/R.Upoor
HFD-550/Chem.ATL/C.Yaciw
HFD-550/Chem.TL/H.Patel
HFD-550/CSO/L.Gorski
HFD-550/Pharm/A.Weir
HFD-550/MO/W.Chambers
HFD-830/DD/C-W.Chen

filename: c:\nda\20369e4

Division of Anti-inflammatory, Analgesic and Ophthalmic Drugs
Review of Chemistry, Manufacturing, and Controls

NDA #: 20-369

REVIEW # 7

DATE OF REVIEW: 12-19-97

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
ORIGINAL SUBMISSION	21-May-93	24-May-93	
AMENDMENT, AZ	20-Jun-97	24-Jun-97	02-Jul-97
AMENDMENT, BI	10-Nov-97	13-Nov-97	See Micro. Review
AMENDMENT, BZ	19-Nov-97	01-Dec-97	08-Dec-97
AMENDMENT, BC	24-Nov-97	28-Nov-97	08-Dec-97
AMENDMENT, BZ	02-Dec-97	02-Dec-97	08-Dec-97

NAME & ADDRESS OF APPLICANT:

Alcon Laboratories, Inc.
6201 South Freeway, R3-14
Fort Worth, Texas 76134.

Contact: Cheryl B. Anderson, Pharm.D.
Manager, Regulatory Affairs
817-551-4325.

DRUG PRODUCT NAME

Proprietary: CILOXAN Ophthalmic Ointment, 0.3% (as ciprofloxacin).
Established: Ciprofloxacin hydrochloride ophthalmic ointment.
Code Name/#: NDC # 00065-0654-35 (From page 4-0248, Volume 4 of 16, dated 6/20/97).
Chem.Type/Ther.Class: 3, Standard Review/Drug Class # 4041322.

PHARMACOLOGIC CATEGORY:

Broad spectrum fluoroquinolone antimicrobial ointment for topical ophthalmic application.

DOSAGE FORM: Sterile Ophthalmic Ointment.

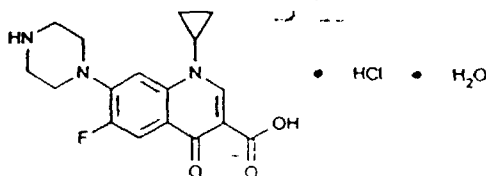
STRENGTHS: 0.3% (as ciprofloxacin base).
0.33% (as ciprofloxacin hydrochloride anhydrous).
0.35% (as ciprofloxacin hydrochloride monohydrate).

ROUTE OF ADMINISTRATION: Topical ophthalmic application.

DISPENSED: X Rx OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA AND WEIGHT:

Ciprofloxacin Hydrochloride (monohydrate).



C₁₇H₁₈FN₃O₃·HCl·H₂O 385.82
3-Quinolincarboxylic acid, 1-cyclopropyl-6-fluoro-1,4-dihydro-
4-oxo-7-(1-piperazinyl)-, monohydrochloride, monohydrate
1-Cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-
quinolincarboxylic acid, monohydrochloride, mono-
hydrate [86393-32-0].

REMARKS:

As per CMC Review # 6 dated 12/17/97, NDA 20-369 was recommended for a **NOT APPROVABLE** action based on the recommendation of the Microbiology Staff of ONDC. Official Overall Recommendation from the CDER Office of Compliance for the preapproval inspections requested for the manufacturing sites was pending at that time.

At this time, CDER EER dated 12/19/97 has been obtained (please see Attachment 1), along with a Memorandum from the Investigations & Preapproval Compliance Branch of the Division of Manufacturing and Product Quality, HFD-324 (please see Attachment 2). For the preapproval inspections requested for this NDA, a **WITHHOLD** Overall Recommendation is made on the basis of evaluation of manufacturing facilities.

CONCLUSIONS & RECOMMENDATIONS:

From the CMC standpoint, this application continues to be recommended for a **NOT APPROVABLE** action based on the recommendation of the Microbiology Staff of ONDC

12/19/1997

Rajendra Upoor, Ph.D., R.Ph.
Review Chemist, HFD-550/830

12-22-97

Hasmukh Patel, Ph.D.
Chemistry Team Leader, HFD-550/830

CC:

Orig. NDA 20-369
HFD-550/Chem/R.Upoor
HFD-805/Micro/B.Uratani
HFD-550/CSO/L.Gorski
HFD-550/MO/W.Chambers

HFD-550/Division File
HFD-550/Chem.TL/H.Patel
HFD-805/Micro/P.Cooney
HFD-550/Pharm/A.Weir
HFD-830/DD/C-W.Chen

filename: c:\nda\20369e5

Division of Anti-inflammatory, Analgesic and
Ophthalmic Drug Products
Review of Chemistry, Manufacturing, and Controls

NDA #: 20-369

REVIEW # 8

DATE OF REVIEW: 03-02-98

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
ORIGINAL SUBMISSION	21-May-93	24-May-93	
AMENDMENT, AZ	20-Jun-97	24-Jun-97	02-Jul-97
AMENDMENT, BI	10-Nov-97	13-Nov-97	See Micro. Review
AMENDMENT, BZ	19-Nov-97	01-Dec-97	08-Dec-97
AMENDMENT, BC	24-Nov-97	28-Nov-97	08-Dec-97
AMENDMENT, BZ	02-Dec-97	02-Dec-97	08-Dec-97
AMENDMENT, AZ	30-Jan-98	03-Feb-98	11-Feb-98

NAME & ADDRESS OF APPLICANT:

Alcon Laboratories, Inc.
6201 South Freeway, R7-18
Fort Worth, Texas 76134.

Contact: Cheryl B. Anderson, Pharm.D.
Manager, Regulatory Affairs
817-551-4325.

DRUG PRODUCT NAME

Proprietary: CILOXAN Ophthalmic Ointment, 0.3% (as ciprofloxacin).

Established: Ciprofloxacin hydrochloride ophthalmic ointment.

Code Name/#: NDC # 00065-0654-35 (From page 0008).

Chem. Type/Ther. Class: 3, Standard Review/Drug Class # 4041322.

PHARMACOLOGIC CATEGORY:

Broad spectrum fluoroquinolone antimicrobial ointment for topical ophthalmic application.

DOSAGE FORM: Sterile Ophthalmic Ointment.

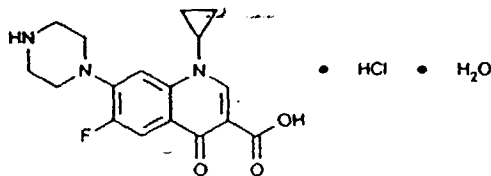
STRENGTHS: 0.3% (as ciprofloxacin base).
0.33% (as ciprofloxacin hydrochloride anhydrous).
0.35% (as ciprofloxacin hydrochloride monohydrate).

ROUTE OF ADMINISTRATION: Topical ophthalmic application.

DISPENSED: X Rx OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA AND WEIGHT:

Ciprofloxacin Hydrochloride (monohydrate).



C₁₇H₁₈FN₃O₃ · HCl · H₂O 385.82
3-Quinolinecarboxylic acid, 1-cyclopropyl-6-fluoro-1,4-dihydro-
4-oxo-7-(1-piperazinyl)-, monohydrochloride, monohydrate
1-Cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-
quinolinecarboxylic acid, monohydrochloride, mono-
hydrate [86393-32-0].

REMARKS:

This CMC Review # 8 is in continuation to previous CMC Review # 7, dated 12/19/97 (and secondary review completed on 12/22/97).

CONCLUSIONS & RECOMMENDATIONS:

Based on data submitted, from the chemistry point of view, this application is recommended for an APPROVAL action, contingent upon satisfactory Microbiology Review, and satisfactory inspection of manufacturing facilities.

Analytical Methods Validation are pending at this time. A paragraph needs to be added in the Action Letter regarding post-approval Methods Validation at the FDA Laboratories for the analytical methods submitted in this application.

03/02/1998

Rajendra Upoor, Ph.D., R.Ph.
Review Chemist, HFD-830/550

3-2-98

Hasmukh Patel, Ph.D.
Chemistry Team Leader, HFD-830/550

cc:

Orig. NDA 20-369
HFD-550/Chem/R.Upoor
HFD-805/Micro/B.Uratani
HFD-550/CSO/L.Gorski
HFD-550/MO/W.Chambers

HFD-550/Division File
HFD-550/Chem.TL/H.Patel
HFD-805/Micro/P.Cooney
HFD-550/Pharm/A.Weir
HFD-830/DD/C-W.Chen

filename: c:\nda\20369r8

Division of Anti-inflammatory, Analgesic and
Ophthalmic Drug Products
Review of Chemistry, Manufacturing, and Controls

NDA #: 20-369

REVIEW # 9

DATE OF REVIEW: 03-24-98

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
ORIGINAL SUBMISSION	21-May-93	24-May-93	
AMENDMENT, AZ	20-Jun-97	24-Jun-97	02-Jul-97
AMENDMENT, BI	10-Nov-97	13-Nov-97	See Micro. Review
AMENDMENT, BZ	19-Nov-97	01-Dec-97	08-Dec-97
AMENDMENT, BC	24-Nov-97	28-Nov-97	08-Dec-97
AMENDMENT, BZ	02-Dec-97	02-Dec-97	08-Dec-97
AMENDMENT, AZ	30-Jan-98	03-Feb-98	11-Feb-98
AMENDMENT, BC	13-Mar-98	16-Mar-98	20-Mar-98

NAME & ADDRESS OF APPLICANT:

Alcon Laboratories, Inc.
6201 South Freeway, R7-18
Fort Worth, Texas 76134.

Contact: Cheryl B. Anderson, Pharm.D.
Manager, Regulatory Affairs
817-551-4325.

DRUG PRODUCT NAME

Proprietary: CILOXAN Ophthalmic Ointment, 0.3% (as ciprofloxacin).
Established: Ciprofloxacin hydrochloride ophthalmic ointment.
Code Name/#: NDC # 00065-0654-35 (From page 0008).
Chem.Type/Ther.Class: 3, Standard Review/Drug Class # 4041322.

PHARMACOLOGIC CATEGORY:

Broad spectrum fluoroquinolone antimicrobial ointment for topical ophthalmic application.

DOSAGE FORM: Sterile Ophthalmic Ointment.

STRENGTHS: 0.3% (as ciprofloxacin base).
0.33% (as ciprofloxacin hydrochloride anhydrous).
0.35% (as ciprofloxacin hydrochloride monohydrate).

ROUTE OF ADMINISTRATION: Topical ophthalmic application.

DISPENSED: X Rx OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA AND WEIGHT:

Ciprofloxacin Hydrochloride (monohydrate).

REMARKS:

This CMC Review # 9 is in continuation to previous CMC Review # 8, dated 03/02/98. This submission authorizes the Agency to cross reference this application for the 483 response in conjunction with the pending supplements for Tobrex® Ophthalmic Ointment (NDA 50-555/S-013), Tobradex® Ophthalmic Ointment (NDA 50-616/S-012), and Maxitrol® Ophthalmic Ointment (NDA 50-065/S-034).

CONCLUSIONS & RECOMMENDATIONS:

From the chemistry point of view, this application continues to be recommended for an APPROVAL action, contingent upon satisfactory Microbiology Review, and satisfactory inspection of manufacturing facilities.

Analytical Methods Validation are pending at this time. A paragraph needs to be added in the Action Letter regarding post-approval Methods Validation at the FDA Laboratories for the analytical methods submitted in this application.

03/24/1998

Rajendra Upoor, Ph.D., R.Ph.
Review Chemist, HFD-830/550

3/24/98

Hasmukh Patel, Ph.D.
Chemistry Team Leader, HFD-830/550

cc:

Orig. NDA 20-369
HFD-550/Chem/R.Upoor
HFD-805/Micro/B.Uratani
HFD-550/CSO/L.Gorski
HFD-550/MO/W.Chambers

HFD-550/Division File
HFD-550/Chem.TL/H.Patel
HFD-805/Micro/P.Cooney
HFD-550/Pharm/A.Weir
HFD-830/DD/C-W.Chen

filename: c:\nda\20369r9.

Division of Anti-inflammatory, Analgesic and
Ophthalmic Drug Products
Review of Chemistry, Manufacturing, and Controls

NDA #: 20-369

REVIEW # 10

DATE OF REVIEW: 03-26-98

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
ORIGINAL SUBMISSION	21-May-93	24-May-93	
AMENDMENT, AZ	20-Jun-97	24-Jun-97	02-Jul-97
AMENDMENT, BI	10-Nov-97	13-Nov-97	See Micro. Review
AMENDMENT, BZ	19-Nov-97	01-Dec-97	08-Dec-97
AMENDMENT, BC	24-Nov-97	28-Nov-97	08-Dec-97
AMENDMENT, BZ	02-Dec-97	02-Dec-97	08-Dec-97
AMENDMENT, AZ	30-Jan-98	03-Feb-98	11-Feb-98
AMENDMENT, BC	13-Mar-98	16-Mar-98	20-Mar-98
AMENDMENT, BC	19-Mar-98	24-Mar-98	26-Mar-98

NAME & ADDRESS OF APPLICANT:

Alcon Laboratories, Inc.
6201 South Freeway, R7-18
Fort Worth, Texas 76134.

Contact: Cheryl B. Anderson, Pharm.D.
Manager, Regulatory Affairs
817-551-4325.

DRUG PRODUCT NAME

Proprietary: CILOXAN Ophthalmic Ointment, 0.3% (as ciprofloxacin).
Established: Ciprofloxacin hydrochloride ophthalmic ointment.
Code Name/#: NDC # 00065-0654-35 (From page 0008).
Chem.Type/Ther.Class: 3, Standard Review/Drug Class # 4041322.

PHARMACOLOGIC CATEGORY:

Broad spectrum fluoroquinolone antimicrobial ointment for topical ophthalmic application.

DOSAGE FORM: Sterile Ophthalmic Ointment.

STRENGTHS: 0.3% (as ciprofloxacin base).
0.33% (as ciprofloxacin hydrochloride anhydrous).
0.35% (as ciprofloxacin hydrochloride monohydrate).

ROUTE OF ADMINISTRATION: Topical ophthalmic application.

DISPENSED: X Rx OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA AND WEIGHT:

Ciprofloxacin Hydrochloride (monohydrate).

REMARKS:

This CMC Review # 10 is in continuation to previous CMC Review # 9, dated 03/24/98, and secondary review completed on 03/25/98. The current submission contains the results of the recent three media fill studies conducted at Alcon Puerto Rico from 01-29-98 to 03-13-98. All the information submitted in the current amendment fall within the purview of a microbiology review. A satisfactory microbiology review is completed for this submission on 24-Mar-98. No chemistry related issues are submitted in the current amendment.

According to EES on-line electronic file data, 23-Mar-98 and 23-Apr-98 are the planned start date and completion dates respectively for pre-approval inspection of manufacturing facilities at Alcon, Puerto Rico.

CONCLUSIONS & RECOMMENDATIONS:

From the chemistry point of view, this application continues to be recommended for an APPROVAL action, contingent upon satisfactory inspection of Alcon Puerto Rico manufacturing facilities.

Analytical Methods Validation are pending at this time. A paragraph needs to be added in the Action Letter regarding post-approval Methods Validation at the FDA Laboratories for the analytical methods submitted in this application.

03/26/1998

Rajendra Upoor, Ph.D., R.Ph.
Review Chemist, HFD-830/550

3-26-98

Hasmukh Patel, Ph.D.
Chemistry Team Leader, HFD-830/550

cc: Orig. NDA 20-369
HFD-550/Chem/R.Upoor
HFD-805/Micro/B.Uratani
HFD-550/CSO/L.Gorski
HFD-550/MO/W.Chambers

HFD-550/Division File
HFD-550/Chem.TL/H.Patel
HFD-805/Micro/P.Cooney
HFD-550/Pharm/A.Weir
HFD-830/DD/C-W.Chen

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