CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-598

CHEMISTRY REVIEW(S)

NDA 21-598

VIGAMOX

Moxifloxacin hydrochloride Ophthalmic Solution, 0.5%

Alcon Laboratories

Su C. Tso, Ph.D.

Division of Anti-inflammatory, Analgesic, and Ophthalmic Drug Products

HFD-550

Table of Contents

Chemistry Review Data Sheet

1. NDA # : 21-598

2. REVIEW #: 1

3. REVIEW DATE: 4/14/03

4. REVIEWER: Su C. Tso, Ph. D.

5. PREVIOUS DOCUMENTS: none

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original	10/15/02
Amendment	11/27/02
NC	12/4/02
Amendment	12/13/02
Amendment	12/17/02
Amendment	1/8/03
Amendment	3/5/03
Amendment	3/11/03
Amendment	4/1/03
Amendment	4/11/03
Amendment	4/14/03

7. **NAME & ADDRESS OF APPLICANT:**

Alcon Inc.
P. O. Box 62
Bosch 69
CH-6331 Hunenburg
Switzerland

US Agent:

Name: Alcon Research, LTD

Address: 6201 s Freeway
Fort Worth, TX. 76134-2099

Representative: Angela C. Kothe, Assistant director, Regulatory Affairs

Chemistry Review Data Sheet

Telephone: 817-551-4933

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: Vigamox
b) Non-Proprietary Name (USAN): Moxifloxacin hydrochloride
c) Code Name/# (ONDC only):
Company or Laboratory Code
AL-15469A (Alcon), BAY 12-8039 (Bayer)
d) Chem. Type/Submission Priority (ONDC only):

- Chem. Type: 3
- Submission Priority: S

1. LEGAL BASIS FOR SUBMISSION:

The NDA is being submitted pursuant to 21 CFR 314.54 and section 505 (b)(1) of the Federal Food, Drug, and Cosmetic Act. The drug product will be marketed as a prescription drug. The application is based upon evidence of safety and effectiveness in the treatment of bacterial conjunctivitis. The product is also unique in being the first non-preserved topical ocular antibiotic; it eliminates the potential for corneal toxicity that has been associated with some antimicrobial preservatives, therefore the product may provide therapeutic advantage. This application is the same as ——— but differs in the "indication", and it is classified as 3S.

10. PHARMACOL. CATEGORY:

Antibacterial agent

11. DOSAGE FORM:

Solution

12. STRENGTH/POTENCY:

0.5%

13. ROUTE OF ADMINISTRATION:

Topical/ocular, one drop in affected eye three times a day.

14. Rx/OTC DISPENSED: x___Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM)[Note25]:

Chemistry Review Data Sheet

_____SPOTS product – Form Completed

__x__Not a SPOTS product

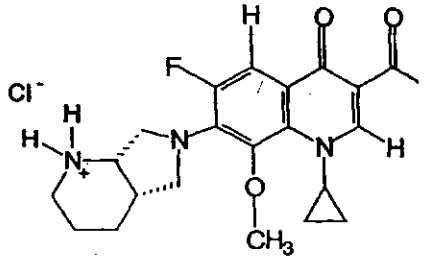
16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name(s)

1-Cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7-[(4aS,7aS)-octahydro-6H-pyrrolol [3,4-b]pyridin-6-yl]-4-oxo-3-quinolinecarboxylic acid, monohydrochloride or

(4aS-cis)-1-Cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7-(octahydro-6H-pyrrolol [3,4-b]pyridin-6-yl)-4-oxo-3-quinolinecarboxylic acid, monohydrochloride

Chemical structure:



Molecular Formula:

C21H24FN304-HCl

Relative Molecular Mass: 437.9

Recommended International Nonproprietary Name (INN): Moxifloxacin

Compendial Name

Moxifloxacin Hydrochloride (USAN)

Other Non-Proprietary Name(s)

1-Cyclopropyl-7-[S,S)-2,8-diazabicyclo[4.3.0] non-8-yl]-6-fluoro-8-methoxy-1,4 - dihydro 4-oxo-3-quinoline carboxylic acid, monohydrochloride

Chemical Abstracts Service (CAS) Registry Number

186826-86-8 (salt)
15109609-2 (base)

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs: Letters of authorization are provided under section P.6 Tab. 1

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
	III			3	Adequate	10/16/00 by Rodriguez, L	6/21/02, LOA
	III			4	Adequate	Not reviewed	8/30/02, LOA
	III			4	Adequate	Not reviewed	9/16/02, LOA
	III			4	Adequate	Not reviewed	9/16/02, LOA 9/13/02 , LOA
	III			3	Adequate	12/6/99 by Tso,S	9/20/02, LOA
	III			3	Adequate	6/25/97 by Srinivasachar, K	98/01/02, LOA
	III			3	Adequate	2/27/98 by Dufffy, Eric (#2)	11/25/02, LOA

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available

7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NDA 21-085	NDA 21-085	LOA dated 9/12/02, current, no outstanding CMC issue, see pg. 10

18. STATUS:

ONDC:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
EES	Pending for inspection	4/2/03	Su Tso
ODS-DMETS	Approval	3/15/03	Denise Toyer
Methods Validation	Pending		
Microbiology	Approval	3/12/02	Bryan Riley

19. ORDER OF REVIEW (OGD Only)

The application submission(s) covered by this review was taken in the date order of receipt.
___ Yes

APPEARS THIS WAY
ON ORIGINAL

The Chemistry Review for NDA 21-598

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The application is recommended for approval from a chemistry, manufacturing, and control standpoint. NDA 21-598 is indicated for bacterial conjunctivitis.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable : None

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Moxifloxacin hydrochloride is a slightly yellow to [redacted] It is a broad-spectrum antibacterial agent. Moxifloxacn hydrochloride has [redacted] (octanol/water); 0.61 (octanol/pH 7 buffer). Moxifloxacin hydrochloride is an approved drug substance for NDA 21-085. The safety profile is described in NDA 21-085. Moxifloxacin hydrochloride is manufactured and supplied by Bayer Corp. Germany. Drug substance manufacturing and control information are referenced in NDA 21-085.

The dosage form is a 0.5% s[redacted]sterile [redacted] solution containing sodium chloride and boric acid; the solution is a [redacted] in color; and it is a broad spectrum antibacterial agent. The drug product is packaged in 3 mL fill in 6 mL natural LDPE bottle (amendment 4/14/03) with white polypropylene cap. The drug product will be manufactured at the ASPEX manufacturing facility, Ft. Worth, TX by Alcon Manufacturing, Ltd. Analytical control procedures are in place at the manufacturing site to ensure quality of the drug product.

B. Description of How the Drug Product is Intended to be Used

The drug product is indicated for treatment of bacterial conjunctivitis, it is to be used [redacted] in the affected eye This application is exactly the same as [redacted]

The dosage form is demonstrated to be stable for 24 months when stored under 2-25 °C. An expiration date of 24 months may be granted for the trade size when stored at 2-25 °C.

C. Basis for Approvability or Not-Approval Recommendation

The drug product composes of 0.5%moxifloxacin, with inactive ingredients being sodium chloride [redacted] and boric acid [redacted]. Drug substance and product specifications were revised; container/closure system deficiencies have been adequately addressed; the dosage form is demonstrated to be stable for 24 months under ambient temperature by stability data; and analytical control procedures are in place at the manufacturing site to ensure quality of the drug product. This NDA is the [redacted]

The application is recommended for approval from chemistry, manufacturing, and control standpoint. [redacted] is not allowed (refer to medical review by Lucious Lim, MD), [redacted] in [redacted], and request that 3 mL fill in 6 mL bottle be approved for both marketing and use as [redacted] Therefore the inspection of the [redacted] facilities for the manufacturing of [redacted] (Alcon Laboratories Inc.,Kaysersberg, France, [redacted]) is not necessary, and the application is recommended for approval from a chemistry, manufacturing, and control standpoint.

The Mock-up container and carton label for the trade size were submitted in amendment dated 4/11/03, it contains the needed information, except the description on the immediate container label is illegible. This deficiency will be addressed by the labeling reviewer, Lisa Hubbard.

III. Administrative

A. Reviewer's Signature

Su C. Tso, Ph. D.

B. Endorsement Block

ChemistName/SuTso
ChemistryTeamLeader/ Linda Ng/

C. CC Block

✓ Page(s) Withheld

61 § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Su Tso
4/15/03 04:50:46 PM
CHEMIST

chemist's review # 1

Linda Ng
4/15/03 04:56:03 PM
CHEMIST

Attachment X

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ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: NDA 21598/000
Stamp: 15-OCT-2002 Regulatory Due: 15-AUG-2003
Applicant: ALCON INC
CH6331
HUNENBERG, , SZ

Priority: 3S Org Code: 550
Action Goal: District Goal: 16-JUN-2003
Brand Name: MOXIFLOXACIN HCL OPHTHALMIC SOL 0.5%
Established Name:
Generic Name: MOXIFLOXACIN HCL OPHTHALMIC SOL 0.5%
Dosage Form: SOL (SOLUTION)
Strength: 0.5%

FDA Contacts: M. PUGLISI (HFD-550) 301-827-2090 , Project Manager
S. TSO (HFD-550) 301-827-2539 , Review Chemist
L. NG (HFD-830) 301-827-2511 , Team Leader

Overall Recommendation:

Establishment: 1610287
ALCON LABORATORIES INC
6201 SOUTH FREEWAY
FORT WORTH, TX 76115

DMF No:
AADA No:

Profile: SNI OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date 10-MAR-2003
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

Responsibilities: FINISHED DOSAGE MANUFACTURER
FINISHED DOSAGE PACKAGER
FINISHED DOSAGE RELEASE TESTER

Establishment: 9615703
ALCON LABORATORIES INC
KAYSERSBERG
KAYSERSBERG, , FR

DMF No:
AADA No:

Profile: SNI OAI Status: NONE
Last Milestone: ASSIGNED INSPECTION TO IB
Milestone Date 10-MAR-2003

Responsibilities: FINISHED DOSAGE LABELER
FINISHED DOSAGE MANUFACTURER
FINISHED DOSAGE PACKAGER

Establishment: [redacted]

DMF No:
AADA No:

Profile: SNI OAI Status: NONE
Last Milestone: ASSIGNED INSPECTION TO IB
Milestone Date 10-MAR-2003

Responsibilities: [redacted]

14-APR-2003

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Establishment: 9610135
BAYER AG

LEVERKUSEN, , GM

DMF No:
AADA No:

Profile: CSN OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date 27-MAR-2003
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

Responsibilities: DRUG SUBSTANCE MANUFACTURER

Establishment: 9610496
BAYER AG
GESCHAFTSBEREICH PHARMA
WUPPERTAL-ELBERFELD, , GM D-4

DMF No:
AADA No:

Profile: CSN OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date 03-MAR-2003
Decision: ACCEPTABLE
Reason: BASED ON PROFILE

Responsibilities: DRUG SUBSTANCE MANUFACTURER

APPEARS THIS WAY
ON ORIGINAL