

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 20-816

CORRESPONDENCE



Food and Drug Administration
Rockville MD 20857

NDA 20-816

DEC 4 1997

Alcon Laboratories, Inc.
Attention: D. Scott Krueger
Director, Regulatory Affairs
P.O. Box 6600
Fort Worth, Texas 76115

Dear Mr. Krueger:

Please refer to your new drug application dated January 26, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for AZOPT (brinzolamide ophthalmic suspension), 1%.

We acknowledge receipt of your submissions and correspondence dated February 10, March 7 and 24, April 24, May 8, and June 5, 12, and 24, 1997.

We have completed the review of this application as submitted with draft labeling, and it is approvable. Before this application may be approved, however, it will be necessary for you to satisfactorily address the following remaining issues:

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TO BE
RELEASABLE

3 pages

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

Any re-submission of this application should include an updated safety report as specified under 21 CFR 314.50 (d)(5)(vi)(b).

In addition, please submit three copies of the introductory promotional material that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to the Division of Anti-Inflammatory, Analgesic and Ophthalmic Drug Products, HFD-550 and two copies of both the promotional material and the package insert directly to:

Division of Drug Marketing, Advertising and Communications, HFD-40
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Within 10 days after the date of this letter, you are required to amend the application, notify us of your intent to file an amendment, or follow one of the other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the application. Any amendment should respond to all of the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

Under 21 CFR 314.102(d) of the new drug regulations, you may request an informal or telephone conference with the Division of Anti-Inflammatory, Analgesic and Ophthalmic Drug Products to discuss what further steps need to be taken before the application may be approved.

If you have any questions, please contact Lissante C. LoBianco, Regulatory Health Project Manager, at (301) 827-2090.

Sincerely,

 2/4/97
Michael Weintraub, M.D.

Director

Office of Drug Evaluation V

Center for Drug Evaluation and Research

Enclosure: Draft Labeling

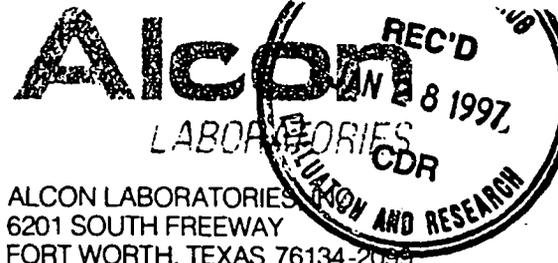
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13 pages

NEW DRUG APPLICATION



Federal Express A/B 3623415530

January 26, 1997

ALCON LABORATORIES
6201 SOUTH FREEWAY
FORT WORTH, TEXAS 76134-2099
(817) 293-0450

Wiley A. Chambers, M.D.
Acting Director, DAAODP, HFD-550
Food and Drug Administration
Central Document Room
Park Building, Room 2-14
12420 Parklawn Drive
Rockville, Maryland 20852



RE: NDA 20-816
Brinzolamide Ophthalmic Suspension 1%
Initial Submission

Dear Dr. Chambers:

Pursuant to the provisions of 21 CFR 314.50, a New Drug Application for AZOPT™ (Brinzolamide Ophthalmic Suspension) 1% is hereby submitted. AZOPT™ is indicated in the treatment of elevated intraocular pressure in patients with ocular hypertension or open-angle glaucoma. Brinzolamide, the active ingredient in AZOPT™, is a potent and selective inhibitor of carbonic anhydrase II enzyme.

This application consists of an Archival and Technical Review copy. The Archival copy consists of 80 volumes and an Index is located in Volume 1. The Technical Review copy consists of sets for

Chemistry	Field Office
Pharmacology	Human Pharmacokinetics
Clinical Data	Microbiology (Product Manufacture)
Statistics	

We are holding three additional copies of the Methods Validation Package and will send these upon FDA's request.

A copy of the Chemistry and Microbiology sections have been sent to the District Office in Dallas, Texas.

Tradename: The tradename AZOPT™ has been selected.

Pagination: The document is consecutively paginated in the lower right hand corner. The page number is made up of two parts, i.e., page 3-245 in which case the "3" represents the item number corresponding to the Chemistry, Manufacturing and Controls section (Form 356h) and "245" is the consecutive page number within the CMC section.

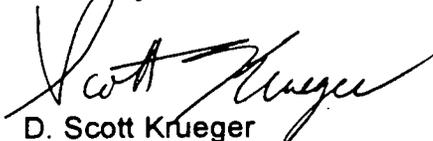
CANDA: A desk copy is being provided which consists of the entire dossier in Wordperfect 5.1 on one CD-ROM. Where the CANDA differs from the hard copy, the reviewer is directed to the hard copy. The Case Report Tabulations are being provided in DOS Lotus 1-2-3 on a second CD-ROM. The clinical biostatistics SAS data sets and programs are also provided electronically on a third CD-ROM. These CDs are being sent to the attention of Ms. Joanne Holmes, Project Manager, along with 16 desk copies of the Summary Section (Archival Volume 1.1).

Safety Information: The cut-off date for the safety data analysis is November 6, 1996.

GLP Compliance Statements: A table is presented on pages 5B- 0072 and 5B-0073 which summarizes the GLP status.

If there are any questions regarding the content or format of the application or CANDA, please contact me at 817/551-8512. If I am not available and you need a prompt response to your inquiry, please contact Dr. Robert Roehrs at the same number.

Sincerely,



D. Scott Krueger
Director, Regulatory Affairs

SK/db
Enclosure

**APPEARS THIS WAY
ON ORIGINAL**

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		Form approved: OMB No. 0910-0001. Expiration Date: December 31, 1995. See OMB Statement on Page 3	
APPLICATION TO MARKET A NEW DRUG FOR HUMAN USE OR AN ANTIBIOTIC DRUG FOR HUMAN USE <i>(TITLE 21, Code of Federal Regulations, 314)</i>		FOR FDA USE ONLY	
		DATE RECEIVED	DATE FILED
		DIVISION ASSIGNED	NDA/ANDA NO. ASS.
NOTE: No application may be filed unless a completed application form has been received (21 CFR Part 314).			
NAME OF APPLICANT		DATE OF SUBMISSION	
Alcon Laboratories, Inc.		January 26, 1997	
ADDRESS (Number, Street, City, State, and Zip Code)		TELEPHONE NO. (Include Area Code)	
Post Office Box 6600 Fort Worth, Texas 76115		(817) 551-8512	
		NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER (If previously issued)	
		NDA 20-816	
DRUG PRODUCT			
ESTABLISHED NAME (e.g., USP/USAN)		PROPRIETARY NAME (If any)	
Brinzolamide		AZOPT	
CODE NAME (If any)		CHEMICAL NAME	
AL-4862			
DOSAGE FORM		ROUTE OF ADMINISTRATION	STRENGTH(S)
Sterile Ophthalmic Suspension		Topical (ocular)	1%
PROPOSED INDICATIONS FOR USE			
Treatment of elevated intraocular pressure and open-angle glaucoma			
LIST NUMBERS OF ALL INVESTIGATIONAL NEW DRUG APPLICATIONS (21 CFR Part 312), NEW DRUG OR ANTIBIOTIC APPLICATIONS (21 CFR Part 314), AND DRUG MASTER FILES (21 CFR 314.420) REFERRED TO IN THIS APPLICATION:			
INFORMATION ON APPLICATION			
TYPE OF APPLICATION (Check one)			
<input checked="" type="checkbox"/> THIS SUBMISSION IS A FULL APPLICATION (21 CFR 314.50)		<input type="checkbox"/> THIS SUBMISSION IS AN ABBREVIATED APPLICATION (ANDA) (21 CFR 314.55)	
IF AN ANDA, IDENTIFY THE APPROVED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION			
NAME OF DRUG		HOLDER OF APPROVED APPLICATION	
TYPE SUBMISSION (Check one)			
<input type="checkbox"/> PRESUBMISSION		<input type="checkbox"/> AN AMENDMENT TO A PENDING APPLICATION	
<input checked="" type="checkbox"/> ORIGINAL APPLICATION		<input type="checkbox"/> RESUBMISSION	
		<input type="checkbox"/> SUPPLEMENTAL APPLICATION	
SPECIFIC REGULATION(S) TO SUPPORT CHANGE OF APPLICATION (e.g., Part 314.70(b)(2)(iv))			
PROPOSED MARKETING STATUS (Check one)			
<input checked="" type="checkbox"/> APPLICATION FOR A PRESCRIPTION DRUG PRODUCT (Rx)		<input type="checkbox"/> APPLICATION FOR AN OVER-THE-COUNTER PRODUCT (OTC)	

HFD-550/11/100

FEB 7 1997

NDA 20-816

Alcon Laboratories, Inc.
Attention: D. Scott Krueger
6201 South Freeway
Fort Worth, Texas 76134-2099

Dear Mr. Krueger:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Azopt (brinzolamide ophthalmic suspension)
Ophthalmic Suspension 1%

Therapeutic Classification: Standard

Date of Application: January 26, 1997

Date of Receipt: January 28, 1997

Our Reference Number: 20-816

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on March 29, 1997, in accordance with 21 CFR 314.101(a).

If you have any questions, please contact Joanne M. Holmes, M.B.A., Clinical Reviewer, at (301) 827-2090.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application.

Sincerely,

/s/

2/7/97

JCL

Lissante C. LoBianco
Acting Supervisor Consumer Safety Officer
Division of Anti-Inflammatory, Analgesic, and
Ophthalmic Drug Products, HFD-550
Office of Drug Evaluation V
Center for Drug Evaluation and Research

NDA 20-816

Page 2

cc:

Original NDA 20-816

HFD-550/Div. Files

HFD-550/Clin Rev/Holmes

HFD-550/SPMS/LoBianco

DISTRICT OFFICE

2/3/97
2/3/97

Drafted by: jh/February 3, 1997/n20816.ack

ACKNOWLEDGEMENT (AC)

**APPEARS THIS WAY
ON ORIGINAL**

BS
ORIG AMENDMENT

Alcon
LABORATORIES

ALCON LABORATORIES, INC.
6201 SOUTH FREEWAY
FORT WORTH, TEXAS 76134-2099
(817) 293-0450

Booze Messenger Service
Federal Express A/B 3623415360

March 7, 1997

Ms. Joanne Holmes
Division of Analgesic, Anti-Inflammatory
and Ophthalmic Drug Products
Center for Drug Evaluation and Research, HFD-550
Food and Drug Administration
Document Control Room
9201 Corporate Boulevard
Rockville, Maryland 20850

REVIEWS COMPLETED	
CSO ACTION:	
<input type="checkbox"/> LETTER	<input type="checkbox"/> N.A.I. <input type="checkbox"/> MEMO
CSO INITIALS	DATE

RE: NDA 20-816
AZOPT (brinzolamide) Ophthalmic Suspension 1%

Dear Ms. Holmes,

Please find enclosed the information requested by the FDA Statistician per your telefacsimile of February 24, 1997 (copy attached).

If you require additional information, please contact me at 817/551-8512.

Sincerely,



D. Scott Krueger
Director, Regulatory Affairs

SK/db
Enclosure



ORIGINAL

Alcon
LABORATORIES

ALCON LABORATORIES, INC.
6201 SOUTH FREEWAY
FORT WORTH, TEXAS 76134-2099
(817) 293-0450

AirBorne A/B 2204145462

June 12, 1997

Division of Analgesic, Anti-Inflammatory
and Ophthalmic Drug Products
Center for Drug Evaluation and Research, HFD-550
Food and Drug Administration
Document Control Room
9201 Corporate Boulevard
Rockville, Maryland 20850

SIX
NDA ORIG AMENDMENT



RE: NDA 20-816
AZOPT (brinzolamide) Ophthalmic Suspension 1%
Four Month Safety Update

Dear Sir or Madam:

Please find enclosed three copies (one Archival, one Clinical Review and one Pharmacology Review) of Part 9, Four Month Safety Update Report for the above referenced NDA which was submitted January 28, 1997. This report covers the period from our last data lockpoint, November 6, 1996 through May 1, 1997.

An electronic (Word Perfect 5.X) copy of the data tables are provided with the clinical review copy.

If there are any questions or comments, please contact me at 817/551-8512.

Sincerely,

D. Scott Krueger
D. Scott Krueger
Director, Regulatory Affairs

DSK/db
Enclosure

REVISIONS COMPLETED

CCO ACTION:
 LETTER IN.A.I. MEMO

CCO INITIALS _____ DATE _____

ORIGINAL

Alcon LABORATORIES

ALCON LABORATORIES, INC.
6201 SOUTH FREEWAY
FORT WORTH, TEXAS 76134-2099
(817) 293-0450

Booze Messenger Service
AirBorne A/B 2204145661

June 24, 1997

BC
NDA ORIG AMENDMENT

Division of Analgesic, Anti-Inflammatory
and Ophthalmic Drug Products
Center for Drug Evaluation and Research, HFD-550
Food and Drug Administration
Document Control Room
9201 Corporate Boulevard
Rockville, Maryland 20850



RE: NDA 20-816
AZOPT (brinzolamide) Ophthalmic Suspension 1%
Stability Update - 12 Month Report

Dear Sir or Madam:

Please find enclosed a report of the 12 month data of our primary stability lots for the above referenced NDA. The conclusion from the analysis of these data are consistent with the data presented in the initial NDA submission. These predict that the product will be stable for at least 24 months when stored at 4° - 30° C.

If there are any questions or comments, please contact me at 817/551-8512.

Sincerely,

D. Scott Krueger
Director, Regulatory Affairs

DSK/db
Enclosure

REVIEWING COMPLETED	
CSD ACTION:	
<input type="checkbox"/> LETTER	<input type="checkbox"/> M.A.I. <input type="checkbox"/> MEMO
GSO INITIALS	DATE

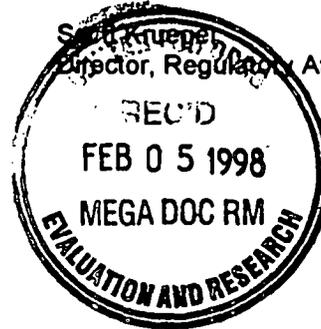
Airborne Express
Airbill No. 9768745055

Alcon
LABORATORIES

February 4, 1998

ALCON LABORATORIES, INC.
6201 SOUTH FREEWAY
FORT WORTH, TEXAS 76134-2099
(817) 293-0450

Wiley Chambers, M.D.
Division of Analgesic, Anti-Inflammatory
and Ophthalmic Drug Products
Center for Drug Evaluation and Research, HFD-550
Food and Drug Administration
Document Control Room
9201 Corporate Blvd.
Rockville, Maryland 20850



RE: NDA 20-816
AZOPT™ Ophthalmic Suspension
Labeling and CMC Amendment

Dear Dr. Chambers:

In follow up to your teleconference with Dr. Gural today, I am confirming that we accept the suggested changes to the package insert and the carton and label texts.

The revised insert text has been provided (Pages 1-4) which reflects the following changes:

<u>Clinical Pharmacology</u>	IOP lowering has been changed to read 4-5mmHg.
<u>Adverse Event</u>	"ocular discharge" has been added under the 1-5% category. "ocular discharge" and ocular pain" have been deleted from the <1% category.
<u>How Supplied</u>	The NDC number for the 2.5 mL commercial package has been corrected to read 0065-0275-24.

Revised carton text for each presentation is provided (Pages 5-9) which reflects the following changes:

<u>Generic Name</u>	Text has been revised to reflect the generic name in lower case letters.
<u>Usual Dosage</u>	The text "Read enclosed insert" has been replaced with "1 drop in the affected eye(s) three times daily".

Container label text for each presentation is provided (Pages 10-14) which reflects the following change:

Generic Name

Text has been revised to present the generic name in lower case letters.

I am also confirming our agreement to the following items:

1. AZOPT™ marketed in the U.S. will utilize the orange cap.
2. An initial expiry period of 12 months is accepted for the 2.5 mL presentations.
3. An initial expiry period of 18 months is accepted for the 5, 10 and 15 mL presentations.
4. The suggestion to test the samples stored in inverted position in the stability protocol commitment at 6-month intervals for the first 2 years and then annually is accepted. A revised Stability Protocol Commitment is provided (Pages 15-16) reflecting this change.
5. Drug Substance Specifications: the specification for _____ and residual solvents has been deleted. A revised specifications page for the drug substance is provided (Page 17).

I have also enclosed an electronic version of the labeling text as a desk copy in Word 6.0.

If I may be of further assistance, please contact me.

Sincerely,


Scott Krueger
Director, Regulatory Affairs

Desk Copies: Dr. Wiley Chambers, Ms. Lissante Lobianco