CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number:	**20706**
Trade Name:	**Emadine**
Generic Name:	**Emedastine difumarate**
Sponsor:	**Alcon Laboratories**
Approval Date:	**December 29, 1997**
Indication:	**Relief of signs and symptoms of allergic conjunctivitis**

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION: 20706

CONTENTS

	Included	Pending Completion	Not Prepared	Not Required
Approval Letter	X			
Tentative Approval Letter				X
Approvable Letter	X			
Final Printed Labeling		X		
Medical Review(s)	X			
Chemistry Review(s)	X			
EA/FONSI	X			
Pharmacology Review(s)	X			
Statistical Review(s)	X			
Microbiology Review(s)				X
Clinical Pharmacology Biopharmaceutics Review(s)	X			
Bioequivalence Review(s)				X
Administrative Document(s)	X			
Correspondence				

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number: 20706

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-706

DEC 29 1997

Alcon Laboratories, Inc.
Attention: Susan H. Caballa
Associate Director, Regulatory Affairs
6201 South Freeway
Fort Worth, Texas 76134-2099

Dear Ms. Caballa:

Please refer to your new drug application dated March 22, 1996, received March 26, 1996, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Emadine™ (emedastine difumarate ophthalmic solution), 0.05%. We also refer to the approvable letter dated February 14, 1997.

We acknowledge receipt of your submissions dated December 16, 1996, and January 3, 6, and 17, February 24, March 11, 17, and 26, October 24, 27, and 28, November 6, and December 2, 9, and 12, 1997.

This new drug application provides for Emadine for the temporary relief of the signs and symptoms of allergic conjunctivitis.

We have completed the review of this application, including the submitted draft labeling, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the draft labeling in the submission dated December 12, 1997, with the revision identified below. Accordingly, the application is approved effective on the date of this letter. As discussed by telephone on December 29, 1997, between Richard Gural of Alcon Laboratories, Inc. and Wiley Chambers and Lissante LoBianco of the Division of Anti-Inflammatory, Analgesic and Ophthalmic Drug Products, the following sentence will be added as the third sentence in the Pregnancy subsection of the Precautions section, "However, at 70,000 times the maximum recommended ocular human use level, emedastine difumarate was shown to increase the incidence of external, visceral and skeletal anomalies in rats."

This revision is a term of the NDA approval. Marketing the product before making the revision, exactly as requested, in the final printed label (FPL) may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FINAL

PRINTED LABELING" for approved NDA 20-706. Approval of this submission by FDA is not required before the labeling is used.

Should additional information relating to the safety and effectiveness of the drug become available, revision of the labeling may be required.

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 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

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Please submit one market package of the drug product when it is available.

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, please contact Lissante C. LoBianco, Regulatory Health Project Manager, at (301) 827-2090.

Sincerely,

MW 12/22/97

Michael Weintraub, M.D.
Director
Office of Drug Evaluation V
Center for Drug Evaluation and Research

cc:
NDA 20-706
HFD-550/Div. Files (with draft labeling)
HFD-002/ORM (with draft labeling)
HFD-92/DDM-DIAB
HFD-550/Deputy Dir/Chambers (with draft labeling) WAC 12/29/97
HFD-550/MO/Ludwig (with draft labeling)
HFD-550/Clin Rev/Holmes (with draft labeling
HFD-550/Acting Supv Proj Mgr/Koerner
HFD-550/PM/LoBianco (with draft labeling) RR 12/29/97
HFD-550/Chem TL/Patel
HFD-550/Chem/Lin
HFD-830/ONDC III/Chen
HFD-550/Pharm TL/Chen
HFD-550/Pharm/Yang
HFD-725/Stat/Patrician
HFD-805/Micro TL/Cooney
HFD-805/Micro/Vincent
HFD-880/Biopharm TL/Bashaw
HFD-105/Office Director
HFD-101/L.Carter
DISTRICT OFFICE
HFD-40/DDMAC (with draft labeling)
HF-2/Medwatch (with draft labeling)
HFD-92/DDM-DIAB (with draft labeling)
HFD-613/OGD (with draft labeling)
HFD-735/DPE (with draft labeling)
HFI-20/Press Office (with draft labeling)

Drafted by: LoBianco/December 10, 1997/20706.ap
Revised by: Chambers/December 15, 1997/n20706ap.wpd
Revised by: LoBianco/December 29, 1997/n20706ap.wpd
APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 20706

APPROVABLE LETTER

NDA 20-706

FEB 14 1997

Alcon Laboratories, Inc.
Attention: Susan H. Caballa
Associate Director, Regulatory Affairs
6201 South Freeway
Fort Worth, Texas 76134-2099

Dear Ms. Caballa:

Please refer to your new drug application dated March 22, 1996, received March 26, 1996, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Emadine™ (emedastine difumarate ophthalmic solution), 0.05%.

We acknowledge receipt of your submissions dated May 1, 22, 29, and 31, June 14, 17, and 25, July 19, August 6, 12, 15, 21, and 23, September 24 and 27, October 31, November 20 and 22, and December 10, 1996.

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 address the following deficiencies:

Redacted 2

pages of trade

secret and/or

confidential

commercial

information

In addition, it will be necessary for you to submit revised draft labeling identical in content to the draft labeling enclosed. If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

Under 21 CFR 314.50(d)(5)(vi)(b), we request that you update your NDA by submitting all safety information you now have regarding your new drug.

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 this Division 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 your other options under 21 CFR 314.110. In the absence of such action FDA may take action to withdraw the application.

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

The drug may not be legally marketed until you have been notified in writing that the application is approved.

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

Sincerely yours,

MWeintraub 2/14/97

Michael Weintraub, M.D.
Director
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Enclosure: Draft Labeling

cc:
Original NDA 20-706
HFD-550/Div. Files
HFD-002/ORM
HFD-92/DDM-DIAB
HFD-550/Acting Div Dir/Chambers VMK 12/31/96
HFD-550/MO/Ludwig EWL 12/31/96
HFD-550/Proj Mgr/Holmes
HFD-550/Acting Supv Proj Mgr/LoBianco 12/31/96
HFD-550/Chem TL/Patel
HFD-820/Chem/Gilman
HFD-550/Pharm TL/Chen
HFD-550/Pharm/Yang
HFD-725/Stat TL/Leung
HFD-725/Stat/Patrician
HFD-805/Micro TL/Cooney
HFD-805/Micro/Vincent
HFD-880/Biopharm TL/Bashaw EWL 12/31/96
HFD-105/Office Director
HFD-101/L.Carter
DISTRICT OFFICE
HFD-40/DDMAC (with draft labeling)

Dra[illegible] by: jl December 13, 1996/20706.ae

APPROVABLE (AE)