CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number:	**20148**
Trade Name:	**Migranal**
Generic Name:	**Dihydroergotamine mesylate**
Sponsor:	**Novartis Pharmaceuticals**
Approval Date:	**December 8, 1997**
Indication:	**Treatment of migraine headaches with and without aura**

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION: 20148

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: 20148

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-148

DEC 8 1997

Novartis Pharmaceuticals Corporation
Attention: Sue Witham
59 Route 10
East Hanover, N.J. 07936-1080

Dear Ms. Witham:

Please refer to your new drug application dated May 17, 1996, received May 17 1996, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Migranal® (dihydroergotamine mesylate, USP) Nasal Spray.

We also acknowledge receipt of the following submissions:

May 15, 1997	June 17, 1997	September 17, 1997
June 9, 1997	August 7, 1997	October 16, 1997
June 13, 1997	September 11, 1997	October 22, 1997

The User Fee goal date for this application is December 10, 1997.

The Indication for this new drug application is as follows:

> Migranal® Nasal Spray is indicated for the acute treatment of migraine headaches with or without aura.

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 enclosed marked-up draft labeling. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed marked-up draft labeling. Marketing the product with FPL that is not identical to this draft labeling 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 20-148. 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 that labeling may be required.

We remind you of your Phase 4 commitments specified in your submission dated June 9, 1997. These commitments, along with any completion dates agreed upon, are listed below.

Please submit the draft and final reports to this NDA as correspondence. In addition, we request under 21 CFR 314.81(b)(2)(vii) that you include in your annual report to this application, a status summary of each commitment. For administrative purposes, all submissions, including labeling supplements, relating to these Phase 4 commitments must be clearly designated "Phase 4 Commitments."

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 Robbin Nighswander, R.Ph., Regulatory Management Officer, at (301) 594-2850.

Sincerely yours,

/S/

Robert Temple, M.D.
Director
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Attachment

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APPLICATION NUMBER: 20148

APPROVABLE LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-148

MAY - 9 1997

Novartis Pharmaceuticals Corporation
Attention: Michael S. Perry, D.V.M., Ph.D.
59 Route 10
East Hanover, N. J. 07936-1080

Dear Dr. Perry:

Please refer to your resubmitted new drug application dated May 17, 1996, received May 17 1996, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Migranal™ (dihydroergotamine mesylate, USP) Nasal Spray.

We also acknowledge receipt of your submissions dated:

May 24, 1996	July 31, 1996	December 20, 1996
June 3, 1996	August 1, 1996	February 12, 1997
July 16, 1996	September 18, 1996	February 14, 1997
July 17, 1996	November 4, 1996(3)	February 19, 1997
July 18, 1996	November 15, 1996	March 13, 1997
July 24, 1996		

The User Fee goal date for this application is May 17, 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 1) adopt as labeling for Migranal™, the draft package insert attached to this letter, modified as requested (i.e., per the notes embedded within the text of the attachment) and 2) commit to provide in phase 4,

Please submit 20 copies of the printed labeling, ten of which are individually mounted on heavy-weight paper or similar material.

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

SAFETY UPDATE

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. Please provide updated information as listed below:

1. Retabulate all safety data including results of trials that were still ongoing at the time of NDA submission. The tabulation can take the same form as in your initial submission. Tables comparing adverse reactions at the time the NDA was submitted vs now will certainly facilitate review.

2. Retabulate drop-outs with new drop-outs identified. Discuss, if appropriate.

3. Provide details of any significant changes or findings, if any.

4. Summarize worldwide experience on the safety of this drug.

5. Submit case report forms for each patient who died during a clinical study or who did not complete a study because of an adverse event.

Please also update the new drug application with respect to reports of relevant safety information, including all deaths and any adverse events that led to discontinuation of the drug and any information suggesting a substantial difference in the rate of occurrence of common but less serious adverse events. The update should cover all studies and uses of the drug including: (1) those involving indications not being sought in the present submission, (2) other dosage forms, and (3) other dose levels, etc.

INTRODUCTORY PROMOTIONAL MATERIAL

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:

Food and Drug Administration
Division of Drug Marketing, Advertising and Communications,
HFD-40
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.