

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20665/S004

CORRESPONDENCE



NDA 20-818

MAR - 6 1998

Novartis Pharmaceuticals Corporation
Attention: Ms. Nancy A. Price
59 Route 10
East Hanover, NJ 07936-1080

Dear Ms. Price:

Please refer to your March 28, 1997 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Diovan HCT (valsartan/hydrochlorothiazide) 80/12.5 and 160/12.5 mg Tablets.

We acknowledge receipt of your submission dated February 24, 1998.

The user fee goal date is August 25, 1998.

This new drug application provides for the use of Diovan HCT Tablets in the treatment of hypertension. This fixed dose combination is not indicated for initial therapy.

We have completed the review of this application and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the final printed labeling included with your February 24, 1998 submission. Accordingly, the application is approved effective on the date of this letter.

We remind you of your Phase 4 commitments specified in your submission dated February 10, 1998. These commitments, along with any completion dates agreed upon, are listed below.

You agreed to reformat the Diovan HCT stability protocol, taking the recommendations from Dr. Stuart Zimmerman's December 19, 1997 facsimile transmission into consideration. In the event that not all recommendations are addressed in the revision, you agreed to include an NDA page reference indicating where the information could be found, or to indicate that it was covered by internal policies or GMPs.

Timeline:

February-March 1998: reformat the Diovan HCT stability protocol

April 1998: resubmit the Diovan HCT stability protocol to the FDA via a prior approval supplement

Protocols, data, and final reports should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. Should an IND not be required to meet your Phase 4 commitments, please submit protocols, data 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. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements, relating to these Phase 4 commitments must be clearly designated "Phase 4 Commitments."

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:

Ms. Kathleen Bongiovanni
Regulatory Health Project Manager
(301) 594-5334

Sincerely yours,

/S/ 3/6/23

Raymond J. Lipicky, M.D.
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc:

Original NDA

HFD-110

HF-2/MedWatch (with labeling)

HFD-002/ORM (with labeling)

HFD-92/DDM-DIAB (with labeling)

HFD-101 (with labeling)

HFD-101/L.Carter

HFD-40/DDMAC (with labeling)

HFD-613/OGD (with labeling)

HFD-735/DPE (with labeling)

DISTRICT OFFICE

HFD-810/ONDC Division Director

HFI-20/Press Office (with labeling)

HFD-110/KBongiovanni

sb/3/4/98;3/6/98

R/D: SZimmerman/3/4/98

JShort/3/4/98

EBarry/3/4/98

ADefelice/3/4/98

EFadiran/3/5/98

AParekh/3/5/98

WNuri/3/5/98

KMahjoob/3/5/98

AWilliams/3/5/98

CGanley/3/5/98

NMorgenstern/3/5/98 *nam 3/6/98*

APPROVAL (AP) (with Phase 4 Commitments)

SPK
3/6/98

Kerry
3-6-98

OS
3/6/98

ADP
3/6/98

ADG
3/6/98
V. Jovanovic/Mohi
3/6/98



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-818

FEB 20 1998

Novartis Pharmaceuticals Corporation
Attention: Ms. Nancy A. Price
59 Route 10
East Hanover, NJ 07936-1080

Dear Ms. Price:

Please refer to your March 28, 1997 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Diovan HCT (valsartan and hydrochlorothiazide) 80/12.5 and 160/12.5 mg Tablets.

We acknowledge receipt of your submissions dated March 28, May 1 and 8, June 25, August 1 and 22, October 13, November 7, and December 11, 12, 16, and 23 (two), 1997; January 14, 15, 21 and 23, February 2, 3, 10 and 13, 1998.

The user fee goal date is March 31, 1998.

We have completed the review of this application as submitted with draft labeling and it is approvable. Before the application may be approved, however, it will be necessary for you to submit final printed labeling (FPL) for the drug. The labeling should be identical in content to the enclosed marked-up draft.

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

We note that in a telephone conversation on February 19, 1998 between Meses. Nancy Price of Novartis and Kathleen Bongiovanni of this Division, you agreed to delete from your carton and container labeling at the time of your next printing. Please note this change in your first annual report.

If additional information relating to the safety or effectiveness of this drug becomes 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 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.

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:

Ms. Kathleen Bongiovanni
Regulatory Health Project Manager
Telephone: (301) 594-5334

Sincerely yours,

Raymond J. Lipicky, M.D.
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure

cc:

~~Original-NDA~~

~~HFD-110~~

HFD-002/ORM

HFD-92/DDM-DIAB

HFD-101

HFD-101/L.Carter

HFD-40/DDMAC (with draft labeling)

DISTRICT OFFICE

HFD-110/KBongiovanni

sb/2/5/98;2/20/98

R/D: SZimmerman/2/17/98

JShort/2/17/98

EBarry/2/18/98

ADeFelice/2/18/98

EFadiran/2/18/98

AParekh/2/18/98

WNuri/2/18/98

KMahjoob/2/18/98

SChun/2/18/98

CGanley/2/18/98

NMorgenstern/2/20/98

APPROVABLE (AE)