DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-818/S-016

Novartis Pharmaceuticals Corporation
Attention: Ms. Nancy A. Price
One Health Plaza
East Hanover, New Jersey 07936-1080

Dear Ms. Price:

Please refer to your supplemental new drug application dated April 11, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Diovan (valsartan/hydrochlorothiazide) 80/12.5, 160/12.5 and 160/25 mg Tablets.

This supplemental new drug application provides for an alternative starting dose of 160 mg.

The **DOSAGE AND ADMINISTRATION** section has been revised to read as follows:

1. The first sentence of this section has been changed to:

   The recommended starting dose of valsartan is 80 mg or 160 mg once daily when used as monotherapy in patients who are not volume depleted.

   In addition, the statement "Patients requiring greater reductions may be started at the higher dose" has been added after the above sentence.

2. Under the subheading entitled "**Dose titration by Clinical Effect"**, the first paragraph has been changed to:

   Diovan HCT tablets contain valsartan and hydrochlorothiazide, 80/12.5 mg, 160/12.5 mg and 160/25 mg. A patient whose blood pressure is not adequately controlled with valsartan monotherapy (see above) may add hydrochlorothiazide by switching to Diovan HCT (valsartan 80 mg/hydrochlorothiazide 12.5 mg or valsartan 160 mg/hydrochlorothiazide 12.5 mg) once daily. If blood pressure remains uncontrolled after about 3-4 weeks of therapy, either valsartan or both components may be increased depending on clinical response. There are no studies evaluating doses of valsartan greater than 160 mg in combination with hydrochlorothiazide 25 mg.

   In addition, the phrase "or valsartan 160 mg/hydrochlorothiazide 12.5 mg" has been added after "Diovan HCT (valsartan 80 mg/hydrochlorothiazide 12.5 mg…)" in the first sentence, second paragraph of this subheading (**Dose titration by Clinical Effect**).

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We have completed the review of this supplemental application 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 submitted final printed labeling (package insert included in your submission of April 11, 2002). Accordingly, the supplemental application is approved effective on the date of this letter.

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:

Mr. Edward Fromm
Regulatory Health Project Manager
(301) 594-5332

Sincerely,

{See appended electronic signature page}

Douglas C.Throckmorton, M.D.
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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

/s/

Doug Throckmorton

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