DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-364/S-028

Novartis Pharmaceuticals Corporation
Attention: Mr. Carl Schlotfeldt
One Health Plaza
East Hanover, New Jersey 07936-1080

Dear Mr. Schlotfeldt:

Please refer to your supplemental new drug application dated July 19, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lotrel (amlodipine besylate and benazepril hydrochloride) 2.5/10, 5/10, 5/20 and 10/20 mg Capsules.

This "Changes Being Effected" supplemental new drug application provides for changes to the **WARNINGS** section of the labeling as follows:

1. Under **WARNINGS**, the ***Angioedema*** subsection was re-titled "***Head and Neck Angioedema***".

2. Following the first paragraph after the ***Head and Neck Angioedema*** subsection, the following text has been added:

> ***Intestinal Angioedema***: Intestinal angioedema has been reported in patients treated with ACE inhibitors. These patients presented with abdominal pain (with and without nausea or vomiting); in some cases there was no prior history of facial angioedema and C-1 esterase levels were normal. The angioedema was diagnosed by procedures

including abdominal CT scan or ultrasound, or at surgery, and symptoms resolved after stopping the ACE inhibitor. Intestinal angioedema should be included in the differential diagnosis of patients on ACE inhibitors presenting with abdominal pain.

We have completed our review of this supplemental new drug application, as amended, and it is approved, effective on the date of this letter, for use as recommended in the final printed labeling (FPL) submitted on July 19, 2004.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

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 call:

Ms. Denise M. Hinton
Regulatory Health Project Manager
(301) 594-5334

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Acting 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/

Norman Stockbridge

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