DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 17-476/S-044 & 045

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

Dear Ms. Price:

Please refer to your supplemental new drug applications (sNDA) dated July 29, 2003 (S-044) and October 2, 2003 (S-045) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Slow-K (potassium chloride) Extended-Release 600 mg Tablets.

We acknowledge receipt of your submissions dated February 9 and June 11, 2004. Your submission dated June 11, 2004 constituted a complete response to our January 28, 2004 action letter.

These "Changes Being Effected" supplemental new drug applications provide for final printed labeling revised in response to our supplement request letters dated February 11, 2003 (S-044) and August 7, 2003 (S-045), as follows:

NDA 17-476/S-044
The following paragraph was added to the end of the OVERDOSAGE section:

The extended release feature means that absorption and toxic effects may be delayed for hours. Consider standard measures to remove any unabsorbed drug.

NDA 17-476/S-045
The following subsection was added to the end of the PRECAUTIONS section:

> Geriatric Use
> Clinical studies of Slow-K tablets did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function, and of concomitant disease or other drug therapy.
>
> This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are

more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

In addition, we note the following revisions in the FPL that were approved in supplement # 025 on January 28, 1986:

1. Under the DESCRIPTION section:
   a. The first paragraph was revised to read:

      Slow-K, potassium chloride extended-release tablets USP, is a sugar-coated (not enteric-coated) tablet for oral administration, containing 600 mg of potassium chloride (equivalent to 8 mEq) in a wax matrix. This formulation is intended to provide an extended-release of potassium from the matrix to minimize the likelihood of producing high, localized concentrations of potassium within the gastrointestinal tract.

   b. The second paragraph, was added as follows:

      Slow-K is an electrolyte replenisher. Its chemical name is potassium chloride, and its structural formula is KCl. Potassium chloride USP is a white, granular powder or colorless crystals. It is odorless and has a saline taste. Its solutions are neutral to litmus. It is freely soluble in water and insoluble in alcohol.

2. Under the CLINICAL PHARMACOLOGY section:
   a. The fourth paragraph, the second sentence was revised to read:

      Such depletion usually develops slowly as a consequence of prolonged therapy with oral diuretics, primary or secondary hyperaldosteronism, diabetic ketoacidosis, severe diarrhea, or inadequate replacement of potassium in patients on prolonged parenteral nutrition.

   b. The following text was added at the end of the section:

      The potassium chloride in Slow-K is completely absorbed before it leaves the small intestine. The wax matrix is not absorbed and is excreted in the feces; in some instance the empty matrices may be noticeable in the stool. When the bioavailability of the potassium ion from Slow-K is compared to that of a true solution the extent of absorption is similar.

      The extended-release properties of Slow-K are demonstrated by the finding that a significant increase in time is required for renal excretion of the first 50% of the Slow-K dose as compared to the solution.

      Increased urinary potassium excretion is first observed 1 hour after administration of Slow-K, reaches a peak at 4 hours, and extends up to 8 hours. Mean daily steady-state plasma levels of potassium following daily administration of Slow-K cannot be distinguished from those following administration of potassium chloride solution or from control plasma levels of potassium ion.

3. Under the INDICATIONS AND USAGE section, first indication, first sentence, the phrase "for the treatment" was changed to "for the therapeutic use."

4. Under PRECAUTIONS, Nursing Mothers, the statement "It is not known if Slow-K has an effect on this content." was added.

5. Under ADVERSE REACTIONS, the statement "Skin rash has been reported rarely." was added.

6. Under DOSAGE AND ADMINISTRATION, the bolded statement "**Note: Slow-K extended-release tablets must be swallowed whole and never crushed, chewed, or sucked."** was added.

We also note the following minor editorial changes:

1. Under the INDICATIONS AND USAGE section, first sentence, the term "controlled-release" was changed to "extended-release."

2. Under the HOW SUPPLIED section:
   b. The NDC numbers were changed to "0078-0320-05" and "0078-0320-09" for the Bottles of 100 and 1000, respectively.
   c. Reference to the "Consumer Pack - One Unit, 12 Bottles – 100 tablets each" and "Accu - Pak® Unit Dose (blister -pack), Box of 100 (strips of 10)" was deleted.
   d. The statement "Samples, when available, are identified by the word SAMPLE appearing on each tablet." was deleted.
   e. The revised date and manufacturer codes were updated.
   f. The manufacturer information was updated to read:

      Distributed by
      Novartis Pharmaceuticals Corporation
      East Hanover, New Jersey 07936

We completed our review of these supplemental new drug applications, as amended, and they are approved, effective on the date of this letter, for use as recommended in the final printed labeling (FPL) submitted on June 11, 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:

Mr. Daryl Allis
Regulatory Project Manager
(301) 594-5332

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

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/s/

Norman Stockbridge

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