DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 19-667/S-050

Novartis Pharmaceuticals Corporation
Attention: Shanthi Ganeshan, PhD
Associate Director, Drug Regulatory Affairs
One Health Plaza
East Hanover, NJ 07936-1080

Dear Dr. Ganeshan:

Please refer to your supplemental new drug application dated March 2, 2005, received March 4, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Sandostatin (octreotide acetate) Injection (Multi-dose Vials and Ampoules).

This supplemental new drug application revises four sections of the package insert (PI), the PRECAUTIONS section – General, Drug Interactions, and Geriatric subsections; and the ADVERSE REACTIONS section – Gastrointestinal subsection.

In the "PRECAUTIONS" section, the "General" subsection, an additional paragraph has been inserted after the second paragraph. The new paragraph states, "In patients with concomitant Type I diabetes mellitus, Sandostatin® Injection and Sandostatin LAR® Depot (octreotide acetate for injectable suspension) are likely to affect glucose regulation, and insulin requirements may be reduced. Symptomatic hypoglycemia, which may be severe, has been reported in these patients. In non-diabetics and Type II diabetics with partially intact insulin reserves, Sandostatin Injection or Sandostatin LAR Depot administration may result in decreases in plasma insulin levels and hyperglycemia. It is therefore recommended that glucose tolerance and antidiabetic treatment be periodically monitored during therapy with these drugs."

In the "PRECAUTIONS" section, the "Drug Interactions" subsection, an additional paragraph has been inserted after the second paragraph. The new paragraph states, "Concomitant administration of octreotide and bromocriptine increases the availability of bromocriptine. Limited published data indicate that somatostatin analogs might decrease the metabolic clearance of compounds known to be metabolized by cytochrome P450 enzymes, which may be due to the suppression of growth hormones. Since it cannot be excluded that octreotide may have this effect, other drugs mainly metabolized by CYP3A4 and which have a low therapeutic index (e.g., quinidine, terfenadine) should therefore be used with caution."

In the "PRECAUTIONS" section, after the "Pediatric Use" subsection, a new subsection has been added, "Geriatric Use." The new paragraph states, "Clinical studies of Sandostatin 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."

In "ADVERSE REACTIONS" section, the "Gastrointestinal" subsection, an additional paragraph states, "In rare instances, gastrointestinal side effects may resemble acute intestinal obstruction, with progressive abdominal distension, severe epigastric pain, abdominal tenderness and guarding."

We completed our review of this supplemental new drug application. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert submitted Match 2, 2005).

Please submit an electronic version of the FPL with the new revision date and product identifier number, according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDAs*. For administrative purposes, designate this submission "**FPL for approved supplement NDA 19-667/S-050.**" Approval of this submission by FDA is not required before the labeling is used.

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 reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Holly Wieland, Regulatory Project Manager, at (301) 827-6410.

Sincerely,

{See appended electronic signature page}

David G. Orloff, MD
Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Research and Evaluation

Enclosure:
Package Insert

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

/s/

Mary Parks
9/2/2005 01:25:59 PM
for Dr. Orloff