DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-008/S-010
NDA 21-008/S-006

Novartis Pharmaceuticals Corporation
Global Regulatory CMC
Attention: Michelle Williams
Associate Director
One Health Plaza
East Hanover, NJ 07936-1080

Dear Ms. Williams:

Please refer to your supplemental new drug applications dated March 31, 2003, received April 1, 2003, (S-010) and September 16, 2002, received September 17, 2002, (S-006), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Sandostatin LAR Depot (octreotide acetate injection) 10 mg, 20 mg and 30 mg vials.

We acknowledge receipt of your submissions dated January 30 and April 12, 2004, for S-006 and your submissions dated December 18, 2003, and April 12, 2004, for S-010.

Your submission of January 30, 2004, constituted a complete response to our March 14, 2003, approvable letter for S-006 and your submission of December 18, 2003, constituted a complete response to our August 3, 2003, approvable letter for S-010.

The **supplemental new drug application, S-006**, provides for revisions to the PRECAUTIONS Section, Drug Interactions and Glucose Metabolism subsections of the package insert as follows:

> Drug Interactions:
> 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 hormone. 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.
>
> Glucose Metabolism:
> In patients with concomitant type I diabetes mellitus, Sandostatin Injection and Sandostatin LAR Depot 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.

The **supplemental new drug application, S-010,** provides for the changes listed below:

1. a new container/closure system (a syringe containing diluent for mixing and injecting Sandostatin LAR)
2. a new manufacturing site
3. additional analytical testing sites
4. a new secondary packaging site
5. an increase in delivery volume from 2 mL to 2.5 mL
6. several manufacturing process changes
7. changes to the package insert: Dosage and Administration, How Supplied, and Storage sections
8. a change to the Patient Instruction booklets to clarify Step 4
9. reformatting the vial labels

We completed our review of these supplemental new drug applications. They are approved, effective on the date of this letter, for use as recommended in the final printed labeling (FPL) submitted on April 12, 2004.

In addition, submit three copies of the introductory promotional materials that you propose to use for these products. Submit all proposed materials in draft or mock-up form, not final print. Send two copies of both the promotional materials and the package inserts directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

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, call Holly Wieland, Regulatory Project Manager, at (301) 827-6410.

Sincerely,

{See appended electronic signature page}

David G. Orloff, M.D.
Director
Division of Metabolic and Endocrine Drug Products, HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosures:

1. Package Insert
2. Container (Vial) Labels (10mg, 20 mg, 30 mg, and demo)
3. Syringe Labels (10mg, 20 mg, 30 mg, and demo)
4. Tray Labels (10mg, 20 mg, 30 mg, and demo)
5. Patient Instruction Booklets (drug product and demo product)

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

/s/

David Orloff

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