DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-386/S-001
NDA 21-223/S-006

Novartis Pharmaceuticals Corporation
One Health Plaza
East Hanover, NJ 07936-1080

Attention: Robert Miranda
Director, Drug Regulatory Affairs

Dear Mr. Miranda:

Please refer to your supplemental new drug applications dated October 16, 2002, received October 17, 2002 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zometa (zoledronic acid) Injection.

Your submission of August 27, 2003 constituted a complete response to our August 14, 2003 action letter.

These supplemental new drug applications provide for the use of Zometa for revised labeling reflecting updated clinical data.

We completed our review of these supplemental applications, as amended. These applications are 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, text for the patient package insert).

Please submit the FPL electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – NDA. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, these submissions should be designated "FPL for approved supplement NDA 21-386/S001 and NDA 21-223/S006." Approval of these submissions by FDA is not required before the labeling is used.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division/ the Division of Metabolic and Endocrine Drug Products and two copies of both the promotional materials and the package insert directly to:

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

Rockville, MD 20857

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 of your postmarketing study commitments in your submission dated February 15, 2002. These commitments are listed below.

1. Conduct a Phase 4 pharmacokinetic, safety and efficacy study in patients with renal dysfunction and serum creatinine > 3 mg/dL. The dose of Zometa to be administered should be adjusted to match the AUC 0-24 h in patients with normal renal function, and safety, efficacy and biomarker suppression should be assessed. A suitable patient population may be patients with multiple myeloma.

Final Report Submission:	Within 29 months of February 22, 2002
Status:	Recruiting now, but final report will probably not be available until 4th quarter 2004

2. Conduct a drug-drug interaction study to evaluate the effect of thalidomide on the pharmacokinetics and safety of Zometa in patients with multiple myeloma.

Final Report Submission:	Within 29 months of February 22, 2002
Status:	On schedule; final report expected July 2004

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to NDA 21-223. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled **"Postmarketing Study Protocol", "Postmarketing Study Final Report", or "Postmarketing Study Correspondence."**

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 Ann Staten, Regulatory Project Manager, at (301) 594-0490.

Sincerely,

{See appended electronic signature page}

Richard Pazdur, M.D.
Director
Division of Oncology Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure: labeling

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

/s/

Richard Pazdur

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