



NDA 21223/S-023

**SUPPLEMENT APPROVAL**

Novartis Pharmaceuticals Corporation  
Attention: Concetta Freund  
Drug Regulatory Affairs  
One Health Plaza  
East Hanover, NJ 07936-1080

Dear Ms. Freund:

Please refer to your Supplemental New Drug Application (sNDA) dated May 08 2012, received May 09, 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Zometa (zoledronic acid) Injection 4 mg/5 mL single dose vial.

We acknowledge receipt of your amendments dated October 2, and November 2, 2012.

This "Prior Approval" supplemental new drug application provides for updates to the package insert to add safety information based on the analysis of safety data from trials for treatment of multiple myeloma and bone metastases from breast, prostate, lung and other solids tumors.

Revisions were proposed to:

1. Section 6 Adverse Reactions, 6.1 Clinical Studies Experience to 1) update the subsection titled "Acute Phase Reactions" and 2) update the "Renal Toxicity" subsection
2. Section 6 Adverse Reactions, 6.2 Postmarketing Experience to 1) add a new subsection titled "Acute Phase Reactions" and 2) update "Hypersensitivity Reactions" subsection to add bronchospasms and interstitial lung disease
3. Section 12 Clinical Pharmacology, 12.3 Pharmacokinetics, Distribution to revise the last paragraph on plasma protein binding

We note that you also included in S-023, [REDACTED] (b) (4) as it relates to the approval of S-022, which provided for revising the package insert to include information on atypical femur fractures and interstitial lung disease. [REDACTED] (b) (4)

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

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to, except with the revisions listed/indicated, the enclosed labeling (text for the package insert, text for the patient package insert, Medication Guide) with the addition of any labeling changes in pending “Changes Being Effectuated” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eLIST may be found in the guidance for industry titled “SPL Standard for Content of Labeling Technical Qs and As” at <http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible via publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes, and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

### **PROMOTIONAL MATERIALS**

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Prescription Drug Promotion (OPDP)  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at <http://www.fda.gov/opacom/morechoices/fdaforms/cder.html>; instructions are provided on page 2 of the form. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

**REPORTING REQUIREMENTS**

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 Elleni Alebachew, Regulatory Project Manager, at (301) 796 5225.

Sincerely,

*{See appended electronic signature page}*

Amna Ibrahim, M.D.  
Deputy Director  
Division of Oncology Products 1  
Office of Hematology and Oncology Products  
Center for Drug Evaluation and Research

ENCLOSURE:  
Content of Labeling

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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AMNA IBRAHIM  
11/09/2012