DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-036/S-035

Novartis Pharmaceuticals Corporation
Attn: Christine Schlotfeldt
Associate Director, Drug Regulatory Affairs
One Health Plaza
East Hanover, New Jersey, 07936-1080

Dear Ms. Schlotfeldt:

Please refer to your supplemental new drug application dated May 8, 2008, received May 9, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Aredia (pamidronate disodium) for injection.

We acknowledge receipt of your submission dated November 24, 2008.

This supplemental new drug application provides for incorporation of new information related to osteonecrosis of the jaw into the following sections of the U.S. prescribing information (USPI):

PRECAUTIONS section

Osteonecrosis of the Jaw subsection

- Revises first and second paragraphs to read:

  Osteonecrosis of the jaw (ONJ) has been reported predominantly in cancer patients treated with intravenous bisphosphonates, including Aredia. Many of these patients were also receiving chemotherapy and corticosteroids which may be risk factors for ONJ. Postmarketing experience and the literature suggest a greater frequency of reports of ONJ based on tumor type (advanced breast cancer, multiple myeloma), and dental status (dental extraction, periodontal disease, local trauma including poorly fitting dentures). Many reports of ONJ involved patients with signs of local infection including osteomyelitis.

  Cancer patients should maintain good oral hygiene and should have a dental examination with preventive dentistry prior to treatment with bisphosphonates.

- Adds "*(See Adverse Reactions)*" to the end of the section.

ADVERSE REACTIONS section

Post-Marketing Experience subsection

- Revises second paragraph to read:

  Cases of osteonecrosis (primarily involving the jaw) have been reported predominantly in cancer patients treated with intravenous bisphosphonates, including Aredia. Many of these patients were also receiving chemotherapy and corticosteroids which may be risk factors for ONJ. Data suggest a greater frequency of reports of ONJ in certain cancers, such as advanced breast cancer and multiple myeloma. The majority of the reported cases are in cancer patients following invasive dental procedures, such as tooth extraction. It is therefore prudent to avoid invasive dental procedures as recovery may be prolonged.(See PRECAUTIONS.)

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and with the minor editorial revisions listed below.

- To the **PRECAUTIONS** section, in the **Renal Insufficiency** subsection, to the first sentence in the second paragraph, change "real" to "renal." (To read: "*In clinical trials, patients with renal impairment (serum creatinine >3.0 mg/dL) have not been studied.*")

- After the **HOW SUPPLIED** section, change the revision date from "REV: November 2007" to "REV: November 2008."

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling (text for the package insert). These revisions are terms of the NDA approval. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission "**SPL for approved NDA 20-036/S-035**."

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
Food and Drug Administration
Suite 12B05
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 Karl Stiller, Regulatory Project Manager in the Division of Reproductive and Urologic Products, at (301) 796-1993.

Sincerely,

{See appended electronic signature page}

Mary H. Parks, M.D.
Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

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