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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-036

OCT 31 1991

Ciba-Geigy Corporation
Attn: John R. Hanagan, M.D.
Vice President, General Drug Development
556 Morris Avenue
Summit, NJ 07901

Dear Dr. Hanagan:

Reference is made to your new drug application dated December 20, 1989, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for Aredia (pamidronate disodium for injection) for Intravenous Infusion.

We also acknowledge receipt of your additional correspondence dated March 15, April 20 and 26, June 5, 6, and 27, July 24, August 3, 8, 10, and 29, September 4, 7, 24, and 28, October 9, November 8, 13, 14, and 21, and December 3 and 4, 1990; and February 5 and 22, March 12 and 20, April 8, May 10 (2) (revised label and carton), 17 (safety update), and 24, June 7 and 27, and 28, September 27, and October 8 and 31 (revised package insert), 1991.

We have completed our review of this application as amended and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the draft labeling. Accordingly, the application is approved, effective on the date of this letter.

Please submit 12 copies of the final printed labeling (FPL) identical to the draft labeling as soon as available. Seven of the copies should be individually mounted on heavy-weight paper or similar material. The submission should be designated for administrative purposes as "FPL for approved NDA 20-036." Approval of the submission by FDA is not required before the labeling is used. Marketing the product with FPL that is not identical to the draft labeling may render the product misbranded and an unapproved new drug.

We note that you agreed in the October 31, 1991, telephone conversation between Mr. Michael Macalush of your firm and Ms. Sharon Olmstead of this Division, to delete "APD" from the fourth line of the carton and vial labels beginning with the next production run. The package insert contained in your October 31, 1991, submission already includes this revision.

We reserve comment as to the adequacy of the methods validation package for Aredia until the results of our laboratory test on the samples submitted are available and have been evaluated. If these results indicate some modifications of the proposed methods are necessary before they can be accepted, or additional samples are required, your cooperation will be expected in finalizing the procedures.

We note that, in your February 22, 1991, submission, you committed to the following Phase 4 actions:

1. Determination of the feasibility of studying Aredia in pediatric patients and performance of studies if determined feasible.

2. Submission of Aredia retreatment data.

3. Examination of the pharmacokinetics of pamidronate after 30, 60 and 90 mg infusions over 4 and 24 hours. (Protocol 09 submitted March 1, 1990.)

We also note in the October 31, 1991, telephone conversation between Mr. Michael Macalush of your firm and Ms. Sharon Olmstead of this Division, we verified your commitment to perform pharmacokinetic studies in patients with renal impairment, as well as in patients with hepatic impairment as stated in your June 5, 1990, correspondence.

In addition, we recommend that you conduct a study in which Aredia therapy would be preceded by the administration of calcitonin. The study design can be discussed further at a later date.

Please submit, in duplicate, the advertising copy that you intend to use in your proposed introductory promotional and/or advertising campaign. Please submit one copy to the Division of Metabolism and Endocrine Drug Products and the second copy to the Division of Drug Marketing, Advertising, and Communications, HFD-240, 5600 Fishers Lane, Rockville, Maryland 20857. Please submit all proposed materials in draft or mock-up form, not final print. Also, please do not use form FD-2253 for this submission; that form is for routine use, not proposed materials.

Please submit one market package of the drug product when available.

We remind you that you must comply with the requirements set forth under 21 CFR 314.80 and 314.81 for an approved NDA.

Sincerely yours,

James Bilstad

James Bilstad, M.D.
Director
Office of Drug Evaluation II
Center for Drug Evaluation and Research