

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**75-290**

**ADMINISTRATIVE DOCUMENTS**

ANDA NUMBER 75-290

FIRM: Bedford Laboratories

DOSAGE FORM: Lyophilized for Injection

STRENGTH: 30 mg/vial and 90 mg/vial

DRUG: Pamidronate Disodium

CGMP STATEMENT/EIR UPDATE STATUS: Acceptable on 11/16/98.  
FUR - Pending.

*EER acceptable  
on 2/26/01  
H. Smola  
2/27/01*

BIO STUDY: The waiver for the requirements for *in vivo* bioequivalence study for the drug product was granted per the Division of Bioequivalence's review dated 4/9/98. DBE has decided not to review the free acid formulation. See note on 12/5/00 Amendment.

METHODS VALIDATION - (DESCRIPTION OF DOSAGE FORM SAME AS FIRM'S):

MV - Pending. (Request dated 1/9/01.) Philadelphia Lab. A post approval commitment has not yet been made.

*Commitment dated 2/20/01  
acceptable*

STABILITY - ARE CONTAINERS USED IN STUDY IDENTICAL TO THOSE IN CONTAINER SECTION? Yes

*H. Smola  
2/26/01*

30 mg/vial

Container  
Closure  
Seal

pe I

1

90 mg/vial

Container  
Closure  
Seal

I

II

24-month CRT (25° ± 2°C/60% ± 5%RH) stability data are provided for Lot 0985-35-108464 (30 mg/vial) and Lot 0987-36-108466 (90 mg/vial).

LABELING: Satisfactory per the November 19, 1999 Approval Summary.

**STERILIZATION VALIDATION (IF APPLICABLE):**

Recommended for approval for issues concerning sterility assurance per the microbiologist November 15, 1999 review.

**SIZE OF BIO BATCH - (FIRM'S SOURCE OF NDS O.K.):** (Yes. 1000)

Exhibit batch 0985-35-108464 (30 mg/vial):

Exhibit batch 0987-36-108466 (90 mg/vial):

**SIZE OF STABILITY BATCHES - (IF DIFFERENT FROM BIO BATCH, WERE THEY MANUFACTURED VIA SAME PROCESS):**

Same Process.

**PROPOSED PRODUCTION BATCH - MANUFACTURING PROCESS THE SAME AS BIO/STABILITY?**

Same Process.

30 mg/vial: 220 liters

90 mg/vial: 140 liters

Review Chemist: Shirley S. Brown  
Team Leader: Michael Smela  
Date: February 16, 2001

2/16/01  
2/16/01

*Shirley S. Brown 2/26/01*

*M. Smela  
2/26/01*

/21/01

**REVIEW OF PROFESSIONAL LABELING  
DIVISION OF LABELING AND PROGRAM SUPPORT  
LABELING REVIEW BRANCH**

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ANDA Number: 75-290      Date of Submission: March 12, 1999

Applicant's Name:      **Bedford Laboratories**

Established Name:      **Pamidronate Disodium For Injection, 30  
mg 60 mg and 90 mg/vial.**

Labeling Deficiencies:

1. CONTAINER            (30 mg, 60 mg and 90 mg)

Satisfactory.

3. CARTON            (1 x 30 mg, 1 x 60 mg, and 1 x 90mg)

Satisfactory.

4. INSERT

- a. GENERAL COMMENT:

Due to changes in the insert labeling for the reference listed drug, AREDIA® (approved September 22, 1998), please revise your insert labeling to be in accord with the enclosed copy of this labeling.

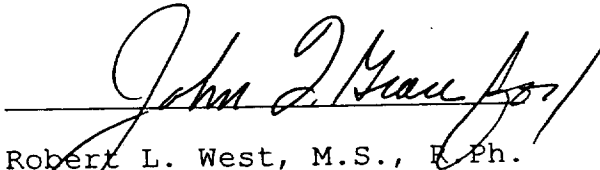
- b. TITLE

We encourage the inclusion of "Rx only" in this section.

Please revise your insert labeling, as instructed above, and submit 12 copies of final printed labels, along with 12 copies of final printed carton and insert labeling.

Please note that we reserve the right to request further changes in your labels and/or labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

A handwritten signature in cursive script, reading "John L. West", written over a horizontal line.

Robert L. West, M.S., R. Ph.  
Director  
Division of Labeling and Program Support  
Office of Generic Drugs  
Center for Drug Evaluation and Research

NDA 20-927  
NDA 20-036/S016

MAR 29 1999

Novartis Pharmaceuticals Corporation  
59 Route 10  
East Hanover, NJ 07936-1080

Attention: Ellen Cutler  
Assistant Director  
Regulatory Affairs

Dear Ms. Cutler:

We acknowledge the receipt of your November 17, 1998 submission containing final printed labeling in response to our September 22, 1998 letter approving your new drug application for Aredia® (pamidronate disodium for injection).

We have reviewed the labeling that you have submitted in accordance with our September 22, 1998 letter, and we find it acceptable.

Should you have any questions, please contact Debra Catterson, Project Manager, at 301-827-1544.

Sincerely yours,

 3-29-99

Robert Justice, M.D.  
Acting Director  
Division of Oncology Drug Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

FDA CDER EES  
ESTABLISHMENT EVALUATION REQUEST  
SUMMARY REPORT

Application: **ANDA 75290/000**  
Stamp: **29-DEC-1997** Regulatory Due:  
Applicant: **BEDFORD LABS**  
**270 NORTHFIELD RD**  
**BEDFORD, OH 44146**

Priority:  
Action Goal:  
Brand Name:  
Established Name: **PAMIDRONATE DISODIUM**  
Generic Name:  
Dosage Form: **INJ (INJECTION)**  
Strength: **30MG;60MG;90MG/VIALS**

Org Code: **600**District Goal: **28-FEB-1999**

FDA Contacts: **ID = 122344**, **Project Manager**  
**M. SMELA JR (HFD-625)** **301-827-5848**, **Team Leader**

Overall Recommendation:

**ACCEPTABLE on 16-NOV-1998 by J. D AMBROGIO (HFD-324) 301-827-0062**

Establishment: **1519257**  
**BEN VENUE LABORATORIES INC**  
**270 & 300 NORTHFIELD RD**  
**BEDFORD, OH 441460568**

DMF No:  
AADA No:

Profile: **SVS** OAI Status: **NONE**  
Last Milestone: **OC RECOMMENDATION**  
Milestone Date: **24-FEB-1998**  
Decision: **ACCEPTABLE**  
Reason: **DISTRICT RECOMMENDATION**

Responsibilities: **FINISHED DOSAGE**  
**MANUFACTURER**

Establishment:

DMF No  
AADA No:

Profile: **CSN** OAI Status: **NONE**  
Last Milestone: **OC RECOMMENDATION**  
Milestone Date: **16-NOV-1998**  
Decision: **ACCEPTABLE**  
Reason: **DISTRICT RECOMMENDATION**

Responsibilities: **DRUG SUBSTANCE**  
**MANUFACTURER**



July 14, 1999

ORIG AMENDMENT

Office of Generic Drugs  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Metro Park II  
7500 Standish Place, Room 150  
Rockville, MD 20855

Ac

**RE:            ANDA 75-290/Response to Microbiology Deficiency**  
**Product:       Pamidronate Disodium for Injection; 30 mg, 60 mg and 90 mg per vials**

Dear Sir:

We wish to amend our abbreviated new drug application 75-290, Pamidronate Disodium for Injection, 30 mg, 60 mg and 90 mg per vial by responding to your letter dated July 6, 1999.

FDA 356h form is provided in Attachment I.

The number associated with the response given below corresponds to the number identifying the deficiencies in the communication.

1.     The pamidronate Disodium does have a bactericidal effect on the organism. The drug product was used to condition the            and the            were            and the challenge was delivered in            The retention validation study using actual drug product solution was conducted by our            The study report is included in Attachment II. Please note that this study report was forwarded to the Agency in our previous response to Major Amendment, dated March 12, 1999.
2.     The bacterial endotoxin testing validation of the drug products for 30 mg/vial and 90 mg/vial is provided in Attachment III, which contains inhibition/enhancement results, determination of noninhibitory concentration, and maximum valid dilution.

If the Agency needs any assistance in the review of this application, the phone numbers for contact are (440)-232-3320, ext.333 (direct) and (440)-232-2772 (fax).

Sincerely,  
for Bedford Laboratories™

Shahid Ahmed  
Director, Regulatory Affairs  
Ben Venue Laboratories, Inc.



A DIVISION OF BEN VENUE LABORATORIES, INC.



**REVIEW OF PROFESSIONAL LABELING  
DIVISION OF LABELING AND PROGRAM SUPPORT  
LABELING REVIEW BRANCH**

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ANDA Number: **75-290**      Date of Submission: **December 23, 1997**

Applicant's Name:    **Bedford Laboratories**

Established Name:    **Pamidronate Disodium For Injection,  
30 mg 60 mg and 90 mg/vial.**

Labeling Deficiencies:

1.    CONTAINER            (30 mg, 60 mg and 90 mg)
  - a.    Delete "/vial" from the expression of strength.
  - b.    Relocate "Do not mix with calcium-containing infusion solutions" to the main panel.
  - c.    Storage temperature recommendation - Reverse the order of the degrees centigrade with degrees Fahrenheit.
  - d.    Replace the "CAUTION: Federal law..." statement with the symbol "Rx only" or "R only". We refer you to the Guidance For Industry, "Implementation of Section 126, Elimination of Certain Labeling Requirements...", at the internet site, <http://www.fda.gov/cder/guidance/index.htm> for guidance.
  
3.    CARTON
  - a.    See comments under CONTAINER.
  - b.    Include a statement of net quantity.
  
4.    INSERT
  - a.    DESCRIPTION  
  
Paragraph one, fourth sentence - Revise to read "Pamidronate disodium" rather than "Pamidronate disodium for injection".

b. CLINICAL PHARMACOLOGY

- i. Hypercalcemia of Malignancy, Clinical Trials  
- Revise to read "etidronate disodium" rather than "Didronel" in the first sentence of paragraph four. In addition, revise throughout the remainder of the entire text of the insert including the tables.
- ii. Osteolytic Bone Metastases of Breast Cancer and Osteolytic Lesions of Multiple Myeloma, Clinical Trials
  - A) Table 1 - Revise "A" to read "Pamidronate disodium" and "P" to read "Placebo".
  - B) Table 2 - Place "PD" in parenthesis following "Pamidronate Disodium".  
[Pamidronate Disodium (PD)]

c. INDICATIONS AND USAGE

Revise to read "Pamidronate disodium for injection" rather than "Pamidronate disodium" in the first sentence of each paragraph.

d. WARNINGS

Revise the first sentence of paragraph three to read "Pamidronate disodium for injection was given...".

e. OVERDOSAGE

Revise to read "given" rather than "give" in the first sentence of paragraph one.

f. DOSAGE AND ADMINISTRATION

i. Hypercalcemia of Malignancy

- A) Moderate Hypercalcemia, paragraph one -  
Revise to read "...pamidronate disodium for injection in...".
- B) Severe Hypercalcemia, last sentence -  
Revise to read as follows:

...(4.0-serum...

ii. Preparation of Solution

- A) Hypercalcemia of Malignancy - Insert "injection" following "sodium chloride" in the second sentence. In addition, revise in the following three paragraphs as well.
- B) Osteolytic Bone Lesions of Multiple Myeloma, last sentence - Insert "and" following "5% dextrose injection".
- C) Last paragraph - See comment c under CONTAINER.

g. HOW SUPPLIED

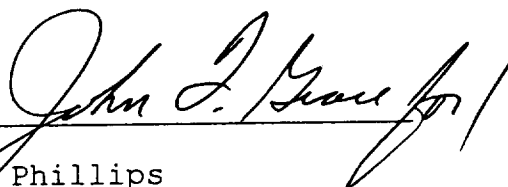
- i. See comments c and d under CONTAINER.
- ii. Insert the following text as the first paragraph:

Pamidronate Disodium for Injection is supplied as follows:...

Please revise your container labels, carton and insert labeling, as instructed above, and submit final printed labels and labeling.

Please note that we reserve the right to request further changes in your labels and/or labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.



Jerry Phillips  
Director  
Division of Labeling and Program Support  
Office of Generic Drugs  
Center for Drug Evaluation and Research