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

EER acceptable on 2/26/01 H Smale 2/27/01

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

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 H Smale 2/26/01

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

30 mg/vial

Container	pe I
Closure	
Seal	

90 mg/vial

Container	
Closure	
Seal	

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.

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	2/16/01
Team Leader:	Michael Smela	2/16/01
Date:	February 16, 2001	

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

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.

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:
Org Code: **600**
Action Goal:
District Goal: **28-FEB-1999**
Brand Name:
Established Name: **PAMIDRONATE DISODIUM**
Generic Name:
Dosage Form: **INJ (INJECTION)**
Strength: **30MG;60MG;90MG/VIALS**

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**

BEDFORD
LABORATORIES™

July 14, 1999

ORIG AMENDMENT

Ac

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

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.

300 Northfield Road • Bedford, Ohio 44146 • (440) 232-3320 • Fax (440) 232-6264

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

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 "℞ 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.

John D. Grace for/

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