CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-290

MICROBIOLOGY REVIEW

REVIEW FOR HFD-617

OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF HFD-805
Microbiologist's Review #2 of ANDA 75-290

November 15, 1999

A. 1. APPLICATION NUMBER: ANDA 75-290

APPLICANT: Bedford Laboratories
300 Northfield Road
Bedford, Ohio 44146
(216) 232-3320
FAX: (216) 232-6264

2. PRODUCT NAME: Pamidronate Disodium for Injection

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: Sterile, lyophilized pamidronate disodium (disodium dihydrogen 3-amino-1-hydroxypropylidene diphosphate), 30 mg (3 mg/mL), 60 mg (6 mg/mL), and 90 mg (9 mg/mL) per vial. For intravenous infusion.

4. METHODS OF STERILIZATION:

5. PHARMALOGICAL CATAGORY and/or PRINCIPLE INDICATION: Pamidronate is an inhibitor of bone resorption, and is indicated for the treatment of moderate or severe hypercalcemia associated with malignancy, with or without bone metastases

B. 1. DATE OF INITIAL SUBMISSION: 12/29/97

2. DATE OF AMENDMENT: 7/14/99

3. DATE OF CONSULT: 9/17/99

4. ASSIGNED FOR REVIEW: 9/24/99

5. RELATED DOCUMENTS: NDA 20-036 (innovator drug)

C. REMARKS: Microbiologist's Review #1 (dated 5/23/99) yielded two deficiencies which were forwarded to the applicant on 7/6/99. The applicant's 7/14/99 response to these deficiencies is the subject of this review (Microbiologist's Review #2).

D. CONCLUSIONS:

The submission is recommended for approval for issues concerning sterility assurance. Specific comments are provided in section "E. Review Notes".

Neal Sweeney 11/15/99

Neal Sweeney, Ph.D.

11/19/99

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Micro Rev.
11/15/99

OFFICE OF GENERIC DRUGS
HFD-600
MICROBIOLOGY REVIEW #1

SUBMISSION:	DOCUMENT DATE:	CDER DATE:	ASSIGNED DATE:
ANDA 75-290	23-DEC-97	29-DEC-97	26-FEB-99

B. ANDA: 75-290 APPLICANT: Bedford Laboratories

DRUG PRODUCT: Pamidronate Disodium for Injection

In reference to your submission dated 23-DEC-97 please respond to the following microbiology deficiencies:

1. A filter retention validation study using actual drug product solution was not included in the application. Please supply a validation report demonstrating the microbial retention capacity of the when used in conjunction with the drug product solution. The validation should involve suspending the challenge organism in the drug product (if the drug product is non-bactericidal), or of the drug product followed and bacterial challenge (if the drug product is bactericidal).

2. No validation or bacterial endotoxin testing of the drug product was provided in the application. Please submit bacterial endotoxin testing validation for Pamidronate Disodium for Injection. The validation should include inhibition/enhancement results, determination of noninhibitory concentration, and maximum valid dilution.

Mary Farming, M.D., Ph.D.
Associate Director of Medical Affairs
Office of Generic Drugs
Center for Drug Evaluation and Research

REVIEW FOR HFD-617

OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF HFD-805
Microbiologist's Review #1 of ANDA 75-290

May 23, 1999

A. 1. **APPLICATION NUMBER:** ANDA 75-290

APPLICANT: Bedford Laboratories
300 Northfield Road
Bedford, Ohio 44146
(216) 232-3320
FAX: (216) 232-6264

2. **PRODUCT NAME:** Pamidronate Disodium for Injection

3. **DOSAGE FORM AND ROUTE OF ADMINISTRATION:** Sterile, lyophilized pamidronate disodium (disodium dihydrogen 3-amino-1-hydroxypropylidene diphosphate), 30 mg, 60 mg, and 90 mg per vial. For intravenous infusion.

4. **METHODS OF STERILIZATION:** [illegible]

5. **PHARMALOGICAL CATAGORY and/or PRINCIPLE INDICATION:** Pamidronate is an inhibitor of bone resorption, and is indicated for the treatment of moderate or severe hypercalcemia associated with malignancy, with or without bone metastases

B. 1. **DATE OF INITIAL SUBMISSION:** 12/29/97

2. **RELATED DOCUMENTS:** NDA 20-036

3. **DATE OF CONSULT:** 2/18/99

4. **ASSIGNED FOR REVIEW:** 2/26/99

C. **REMARKS:** Innovator product is Aredia® held by Novartis, NDA 20-036.

D. CONCLUSIONS:

The submission is approvable pending resolution of microbiology issues concerning sterility assurance. Specific comments are provided in section "E. Review Notes". See "List of Microbiology Deficiencies and Comments" which should be provided to the applicant.

Neal Sweeney 5/23/99

Neal Sweeney, Ph.D.

PAC 5/24/99

MT 6/10/99

cc:

eeney

May 23, 1999

May 23, 1999

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Micro Review
5/23/99