CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 21-223

MICROBIOLOGY REVIEW(S)

MAY 22 2000

REVIEW FOR HFD-510
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW #2 of NDA 21-223
22 May 2000

A. 1. NDA 21-223

APPLICANT: Novartis Pharmaceutical Corporation
59 Route 10
East Hanover, NJ 07936-1080

2. PRODUCT NAME: Zometa® (zoledronic acid for injection)

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:
The product is supplied as a lyophilized powder for reconstitution. Each vial supplies 4 mg of zoledronic acid.

4. METHODS OF STERILIZATION:
The product is

5. PHARMACOLOGICAL CATEGORY and/or PRINCIPLE INDICATION:
The product is indicated in the treatment of tumor induced hypercalcemia.

B. 1. DATE OF INITIAL SUBMISSION: 21 December 1999

2. DATE OF AMENDMENT: 17 May 2000 (Subject of this Review)

3. RELATED DOCUMENTS: (none)

4. DATE OF CONSULT: 10 January 2000

C. REMARKS: The submission provides for manufacture, quality control, and packaging of the drug product at:

Novartis Pharma Stein AG
Schaffhauserstrasse
CH-4332 Stein
Switzerland

This amendment review was completed using a desk copy of the applicant's response provided directly to the reviewer.

D. CONCLUSIONS: The application is recommended for approval on the basis of sterility assurance.

/S/ 22 May 2000

Paul Stinavage, Ph.D.

cc: Original NDA 21-223
HFD-510/R. Hedin/Division File
HFD-805/Consult File/Stinavage

Drafted by: P. Stinavage, 22 May 2000
R/D initialed by P. Cooney

/S/ for PHC 5-22-2000

APPEARS THIS WAY
ON ORIGINAL

APR 13 2000

REVIEW FOR HFD-510
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW #1 of NDA 21-223
13 April 2000

A. 1. NDA 21-223

APPLICANT: Novartis Pharmaceutical Corporation
59 Route 10
East Hanover, NJ 07936-1080

2. PRODUCT NAME: Zometa® (zoledronic acid for injection)

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:
The product is supplied as a lyophilized powder for reconstitution. Each vial supplies 4 mg of zoledronic acid.

4. METHODS OF STERILIZATION:
The product is [redacted]

5. PHARMACOLOGICAL CATEGORY and/or PRINCIPLE INDICATION:
The product is indicated in the treatment of tumor induced hypercalcemia.

B. 1. DATE OF INITIAL SUBMISSION: 21 December 1999

2. DATE OF AMENDMENT: (none)

3. RELATED DOCUMENTS: (none)

4. DATE OF CONSULT: 10 January 2000

C. REMARKS: The submission provides for manufacture, quality control, and packaging of the drug product at:

Novartis Pharma Stein AG
Schaffhauserstrasse
CH-4332 Stein
Switzerland

APPEARS THIS WAY
ON ORIGINAL

D. CONCLUSIONS: The application is approvable pending resolution of microbiology concerns.

/S/ 13 April 2000
Paul Stinavage, Ph.D.

/S/ 4/13/00

cc: Original NDA 21-223
HFD-510/R. Hedin/Division File
HFD-805/Consult File/Stinavage

Drafted by: P. Stinavage, 13 April 2000
R/D initialed by P. Cooney

APPEARS THIS WAY
ON ORIGINAL

MEMORANDUM
Sept. 19, 2000

TO: File
FROM: Kenneth L. Hastings, Dr.P.H.
Acting Associate Director for Pharmacology and Toxicology, ODE II
SUBJECT: NDA 21-223 (Zoledronic acid for injection; ZOMETA®)

I have read the Pharmacology/Toxicology review and supporting documents and concur with the conclusions. In particular, please refer to the product label as proposed by the Sponsor. The wording in the **Carcinogenicity/Mutagenesis/Impairment of Fertility** and **Pregnancy Category** sections should be considered inadequate. On pages 95 and 96 of the Pharmacology/Toxicology review, Drs. Gemma Kuijpers, Fred Alavi, and John Gong have proposed alternative wording for the label and Dr. Jeri El-Hage concurred. I believe the wording proposed by the review team is accurate and should used in the product label.

/S/
Kenneth L. Hastings, Dr.P.H.

APPEARS THIS WAY
ON ORIGINAL