CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-841

BIOEQUIVALENCE REVIEW(S)

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75-841 APPLICANT: Whitney Pharmaceuticals Inc.

DRUG PRODUCT: Pamidronate disodium 3 mg/ml, 6 mg/ml and 9 mg/ml injection

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

for Dale P. Conner, Pharm. D.
Director
Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

CC: ANDA 75-841
ANDA DUPLICATE
DIVISION FILE
HFD-651/ Bio Drug File
HFD-650/ Reviewer

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Printed in final on / /

Endorsements: (Final with Dates)
HFD-655/ JLee C.S. 7/11/00
HFD-655/ Bio team Leader
HFD-650/ D. Conner for RWP 8/10/2000

7/12/00

BIOEQUIVALENCY - ACCEPTABLE submission date: Feb 28, 2000

6.	**WAIVER** (WAI)	Strengths: 3 mg/ml **Outcome: AC**
6.	**WAIVER** (WAI)	Strengths: 6 mg/ml **Outcome: AC**
6.	**WAIVER** (WAI)	Strengths: 9 mg/ml **Outcome: AC**

Outcome: AC
Outcome Decisions: **AC** - Acceptable

WinBio Comments:
Waivers are granted under 21 CFR 320.22 (b)(1)

APPEARS THIS WAY
ON ORIGINAL

Pamidronate Disodium Injection
3 mg/ml, 6 mg/ml and 9 mg/ml (10 ml vials)
ANDA #75-841
Reviewer: J. Lee
75841W.200

Whitney Pharmaceuticals Inc.
Vienna, Virginia
Submission date:
February 28, 2000
~~April 19, 2000 (accepted for filing)~~

Review of 3 Requests for Waiver

The sponsor has submitted an application for pamidronate disodium 3 mg/ml, 6 mg/ml and 9 mg/ml injection and is requesting waiver of in-vivo requirements under 21 CFR 320.22 (b)(1).

This application was received under a suitability petition (99P-2252/CP1; app. 04/18/00) allowing for a change in dosage form from that of the listed drug products (Aredia®). Aredia® products (Novartis) are lyophilized products to be reconstituted prior to use, while Whitney products are ready to use solutions.

Pamidronate disodium is a bone-resorption inhibitor.

Listed below is a formulation comparison of the test and reference products:

	Whitney per vial	Aredia® per vial	
Pamidronate disodium	- - - - -	30 mg	
Pamidronic acid	———	- - - -	
	(eq. 30 mg pamidronate Na_2[1])		
Phosphoric acid	adj pH.	adj. pH	
NaOH	———	- - -	***3 mg/ml vial***
Mannitol	470 mg	470 mg	
Water for Injection	qs 10 ml	qs 10 ml	
Pamidronate disodium	- - - - -	60 mg	
Pamidronic acid	———	- - - -	
	(eq. 60 mg pamidronate Na_2[1])		
Phosphoric acid	adj. pH	adj. pH	
NaOH	———	- - -	***6 mg/ml vial***
Mannitol	400 mg	400 mg	
Water for Injection	qs 10 ml	qs 10 ml	
Pamidronate disodium	- - - - -	90 mg	
Pamidronic acid	———	- - - -	
	(eq. 90 mg pamidronate Na_2[1])		
Phosphoric acid	adj. pH	adj. pH	
NaOH	———	- - -	***9 mg/ml vial***
Mannitol	375 mg	375 mg	
Water for Injection	qs 10 ml	qs 10 ml	

[1] Formed by in-situ reaction between pamidronic acid and NaOH
Phosphoric acid used for pH adjustment

Comment:

1. The formulations are identical except that Aredia® does not list NaOH as having been used in pH adjustment. Formulations do not have to be identical if the generic product is accepted for filing under a suitability petition. Upon approval, the Whitney products will receive an RLD (+) designation.

Recommendation:

1. The Division of Bioequivalence finds that the information submitted by Whitney Pharmaceuticals Inc. demonstrates that pamidronate disodium 3 mg/ml, 6 mg/ml and 9 mg/ml injection falls under 21 CFR 320.24 (b)(6) of Bioavailability/Bioequivalence Regulations.

2. From the Bioequivalence standpoint, this application is acceptable.

R. Lee 7/11/00

J. Lee
Division of Bioequivalence
Review Branch II

RD INITIALED SNERURKAR
FT INITIALED SNERURKAR _____ 7/12/2000

Concur: _____ Date: 8/10/2000

for Dale Conner, Pharm. D.
Director, Division of Bioequivalence

JLee/jl/07-11-00

cc: NDA #75-841 (original, duplicate), HFD-630, HFD-655 (Lee, Patnaik), Drug File, Division File

APPEARS THIS WAY
ON ORIGINAL

Note:
The issue of non-Q and Q in inactive ingredients for injectables in applications received under a suitability petition was discussed with Don Hare and other members of the regulatory review branch in June, 2000. Generics do not have to be Q and Q with the innovator since they will not be deemed bioequivalent to the innovator product(s).

OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE

ANDA #: 75-841 SPONSOR: Whitney Pharmaceuticals

DRUG AND DOSAGE FORM: Pamidronate disodium Inj

STRENGTH(S): 3mg/ml, 6 mg/ml, 9 mg/ml

TYPES OF STUDIES: N/A

CLINICAL STUDY SITE(S): N/A

ANALYTICAL SITE(S): N/A

~~STUDY~~ SUMMARY: Accepted under 21 CFR 320.24 (b)(6)

DISSOLUTION: N/A

DSI INSPECTION STATUS

Inspection needed: YES (NO)	Inspection status:	Inspection results:
First Generic ~~No~~ Yes (NEW RLD)	Inspection requested: (date)	
New facility _____	Inspection completed: (date)	
For cause _____		
Other _____		

PRIMARY REVIEWER: J. Lee BRANCH: II

INITIAL: J. L. DATE: 7/11/00

TEAM LEADER: SG Nerurkar BRANCH: II

INITIAL: [signature] DATE: 7/12/2000

for DIRECTOR, DIVISION OF BIOEQUIVALENCE: DALE P. CONNER, Pharm. D.

INITIAL: [signature] DATE: 8/10/2000