

**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,



*fr*

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

V:\FIRMSnz\Whitney\ltrs&rev\75841W.200  
Printed in final on / /

Endorsements: (Final with Dates)

HFD-655/ JLee *L.P. 7/11/00*

HFD-655/ Bio team Leader

HFD-650/ D. Conner *for Rev 8/10/2000*

*[Handwritten signature]* 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:

	<u>Whitney</u> per vial	<u>Aredia®</u> per vial	
Pamidronate disodium	-----	30 mg	
Pamidronic acid	-----	-----	
	(eq. 30 mg pamidronate Na <sub>2</sub> <sup>1</sup> )		
Phosphoric acid	adj. pH.	adj. pH	
NaOH	-----	---	<i>3 mg/ml vial</i>
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 <sub>2</sub> <sup>1</sup> )		
Phosphoric acid	adj. pH	adj. pH	
NaOH	-----	---	<i>6 mg/ml vial</i>
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 <sub>2</sub> <sup>1</sup> )		
Phosphoric acid	adj. pH	adj. pH	
NaOH	-----	---	<i>9 mg/ml vial</i>
Mannitol	375 mg	375 mg	
Water for Injection	qs 10 ml	qs 10 ml	

<sup>1</sup> 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.

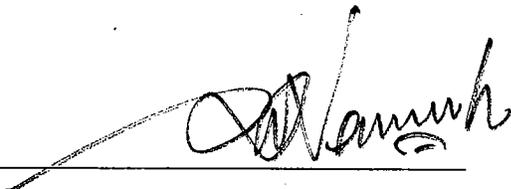
Recommendation:

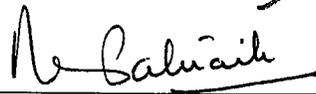
1. The Division of Bioequivalence finds that the information submitted by Whitney Pharmaceuticals Inc. demonstrates that pamidronate disodium 3 mg/ml, 6 mg/ml and 9 mg/ml injection falls under 21 CFR 320.24 (b)(6) of Bioavailability/Bioequivalence Regulations.
2. From the Bioequivalence standpoint, this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

 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).

**APPEARS THIS WAY  
ON ORIGINAL**

**OFFICE OF GENERIC DRUGS  
DIVISION OF BIOEQUIVALENCE**

ANDA #: 75-841

SPONSOR: Whitney Pharmaceuticals

DRUG AND DOSAGE FORM: Pamidronate disodium Inj

STRENGTH(S): 3mg/ml, 6mg/ml, 9mg/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 <input type="checkbox"/> NO <input checked="" type="checkbox"/>	Inspection status:	Inspection results:
First Generic <input type="checkbox"/> No <input type="checkbox"/> Yes <input type="checkbox"/> <small>NEW RLD</small>	Inspection requested: (date)	
New facility <input type="checkbox"/>	Inspection completed: (date)	
For cause <input type="checkbox"/>		
Other <input type="checkbox"/>		

PRIMARY REVIEWER: J. Lee

BRANCH: II

INITIAL: J. P.

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: D. Conner

DATE: 8/10/2000