

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
76394

BIOEQUIVALENCY REVIEW(S)

**OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE**

ANDA #: 76-394

SPONSOR : Apotex Corporation

DRUG AND DOSAGE FORM : Amiodarone HCl Injection

STRENGTH(S) : 50 mg/mL, 3 mL single dose vial.

TYPES OF STUDIES : SD

SDF

MULT

OTHER

CLINICAL STUDY SITE(S) : N/A

ANALYTICAL SITE(S) : N/A

STUDY SUMMARY : N/A

DISSOLUTION : N/A

DSI INSPECTION STATUS

Inspection needed: YES / <input type="checkbox"/> NO	Inspection status:	Inspection results:
First Generic _____	Inspection requested: (date)	
New facility _____	Inspection completed: (date)	
For cause _____		
Other _____		

PRIMARY REVIEWER : MAMATA S. GOKHALE, Ph.D. BRANCH : III

INITIAL : msgh DATE : 7/18/02

TEAM LEADER : GJP SINGH, Ph.D. BRANCH : III

INITIAL : /S/ DATE : 7/18/02

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

INITIAL : /S/ DATE : 7/29/2002

Amiodarone HCl Injection
50 mg/mL; 3 mL Single Dose Vial
ANDA # 76-394
Reviewer: Mamata S. Gokhale

Apotex Corporation
50 Lakeview Parkway
Suite 127
Vernon Hills, IL 60061
Submission Date: April 4, 2002

Review of a Waiver Request

Background

1) The firm has submitted a request for a waiver of in vivo bioavailability/bioequivalence study requirements based on 21 CFR 320.22 (b) (1) for its proposed product, Amiodarone HCl Injection, 50 mg/mL. The RLD is Cordarone® Intravenous Injection, 50 mg/mL (NDA 20-377), manufactured by Wyeth Ayerst Laboratories, Inc.

2) Amiodarone HCl is a class III antiarrhythmic drug indicated for initiation of treatment and prophylaxis of frequently recurring ventricular fibrillation and hemodynamically unstable ventricular tachycardia in patients refractory to other therapy. Amiodarone is sparingly soluble in water.

3) The RLD, Cordarone® Intravenous Injection is a sterile clear, pale-yellow solution visually free from particulates. It is available in packages of 10 ampuls, 3 mL each. The test product, Amiodarone HCl Injection, 50 mg/mL, is also a sterile clear, pale-yellow solution to be administered by intravenous route and is supplied in 3 mL single dose vials.

4) The DBE has previously granted several waiver requests for Amiodarone HCl Injection, 50 mg/mL.

Formulation Comparison

Ingredient	^{1,2} Reference Product mg/mL	² Test Product mg/mL
³ Amiodarone HCl	50 ✓	50
Benzyl Alcohol, NF	20.2 ✓	20.2
Polysorbate 80, NF	100 ✓	100
Water for Injection, USP/EP	Q.S. ✓	Q.S.

¹Confirmed from the FDA's COMIS database, PDR 2002 and the DBE reviews of ANDA 75-955, 76-163

²The test and reference products are clear yellow solutions (physical property).

³Active ingredient

Comments

The test product is eligible for a waiver of bioequivalence study requirements because;

- 1) It is a parenteral solution intended for administration solely by injection by the intravenous route.
- 2) Active ingredient, route of administration, dosage form and strength of the test product are same as those of the reference listed product.
- 3) Inactive ingredients in the test and reference products are qualitatively and quantitatively the same.

Recommendation

The Division of Bioequivalence agrees that the information submitted by Apotex Corporation demonstrates that Amiodarone HCl Injection, 50 mg/mL, 3 mL Single Dose Vial falls under 21 CFR 320.22(b) (1) (i) (ii) of the Bioavailability/Bioequivalence regulations. The waiver of an *in vivo* bioequivalence study requirements for Amiodarone HCl Injection, 50 mg/mL, 3 mL Single Dose Vial is granted. From the bioequivalence point of view, the Division of Bioequivalence deems the test product to be bioequivalent to Cordarone® Intravenous Injection, 50 mg/mL, 3 mL Single Dose Vial, manufactured by Wyeth-Ayerst Laboratories, Inc.

Mamata S. Gokhale, Ph.D.
Review Branch III
Division of Bioequivalence

ISI

7/18/02

RD INITIALED GJP Singh, Ph.D.
FT INITIALED GJP Singh, Ph.D.

ISI

Date 7/8/02

Concur:

ISI

Date 7/29/2002

for

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

cc:

ANDA# 76-394 (original, duplicate), Gokhale, HFD-658, Makary, HFD-658, Drug File, Division File

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA # 76-394

APPLICANT: Apotex Corporation

DRUG PRODUCT: Amiodarone HCl Injection
50 mg/mL; 3 mL Single Dose Vial

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,

/S/

for

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

CC: ANDA # 76-394
 ANDA DUPLICATE
 DIVISION FILE
 HFD-651/ Bio Drug File
 HFD-658/ Reviewer: M. Gokhale

Printed in final on 7/08/02

Endorsments: (Final with Dates)

HFD-658/ M. Gokhale *MGK 7/8/02*
HFD-658/ GJP. Singh *GJS 7/8/02*
HFD-650/ D. Conner *for Rev 7/24/2002*
HFD-617/ S. Mazzella

Bioequivalency- Acceptable

Submission Date: 4 April, 2002

Waiver (WAI)

Strength: 50 mg/mL, 3 mL single dose vial
Outcome: AC

Outcome Decisions: AC- Acceptable
Winbio comments: Waiver is granted