

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
ANDA 77155

Name: Fenoldopam Mesylate, 10 mg (base)/mL

Sponsor: Sandoz Pharmaceuticals, Inc.

Approval Date: February 15, 2005

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
ANDA 77155

CONTENTS

Reviews / Information Included in this Review
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Approval Letter	X
Other Action Letters	
Labeling	X
Labeling Review(s)	X
Medical Review(s)	
Chemistry Review(s)	X
Pharm/Tox Review(s)	
Statistical Review(s)	
Microbiology Review(s)	X
Bioequivalence Review(s)	X
Other Review(s)	
Administrative & Correspondence Documents	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 77155

APPROVAL LETTER

FEB 15 2005

Sandoz Pharmaceuticals, Inc.
Attention: Beth Brannan
Director of Regulatory Affairs
U.S. Agent for: Sabex 2002 Inc.
2555 W. Midway Blvd.
P.O. Box 446
Broomfield, CO 80038

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated May 20, 2004, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Fenoldopam Mesylate Injection USP, 10 mg (base)/mL packaged in 10 mg (base)/1 mL and 20 mg (base)/2 mL single-dose ampules.

Reference is also made to your amendments dated November 2, November 3, November 19, and December 16, 2004; and January 13, and January 27, 2005 (two submissions).

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly the application is approved. The Division of Bioequivalence has determined your Fenoldopam Mesylate Injection USP, 10 mg (base)/mL, to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Corlopan[®] Injection USP, 10 mg (base)/mL, of Hospira Inc.

Under Section 506A of the Act, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

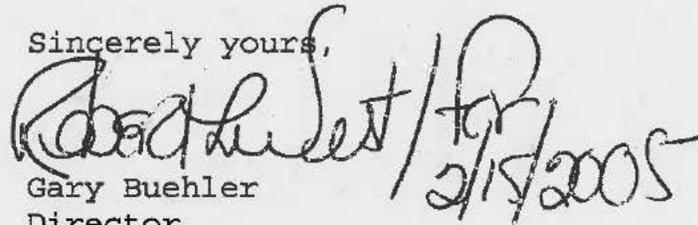
Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert(s) directly to:

Food and Drug Administration
Division of Drug Marketing, Advertising, and Communications, HFD-42
5600 Fishers Lane
Rockville, MD 20857

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Division of Drug Marketing, Advertising, and Communications (HFD-42) with a completed Form FDA 2253 at the time of their initial use.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Gary Buehler", followed by a vertical line and the date "2/15/2005".

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 77-155
Division File
Field Copy
HFD-610/R. West
HFD-205
HFD-610/Orange Book Staff

Endorsements:

HFD-620/Y. Amin/

HFD-623/A. Mueller/

HFD-617/S. Eng/

HFD-613/J. Barlow/

HFD-613/J. Grace/

Y. Amin 1/6/05

A. Mueller 1-6-05

S. Eng 1/5/2005

J. Barlow 1/24/05

R. West 2/15/2005

1/24/2005

PS 2/11/05

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F/T by SE

APPROVAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 77155

LABELING

Section III.

Labeling

A. Current Labeling

Final Printed Labels
ANDA 77-155
Carton: 1 mL (10 mg/mL) ampoule

NDC 0781-3005-71
Fenoldopam
Mesylate
Injection, USP

Brookfield, CO 80020

10 mg/mL



Manufactured in Canada by
Sandoz Canada Inc.
Distributed by
Lake Pharmaceutical, Inc.
an affiliate of Sandoz Inc.

**Fenoldopam Mesylate
Injection, USP**
10 mg/mL

Brookfield, CO 80020

**Fenoldopam Mesylate
Injection, USP**
10 mg/mL

Warnings: Dilute before administering. Inspect visually
for particulate matter.

Store at 2° to 30°C.

Each mL contains citric acid 3.44 mg, fenoldopam
mesylate equivalent to fenoldopam 10 mg, propylene
glycol 51.8 mg, sodium citrate dihydrate 0.61 mg,
sodium metabisulfite 1 mg, and water for injection; pH
range of 2.8 to 3.8.

Usual Dosage: See package insert.

NDC 0781-3005-71

**Fenoldopam Mesylate
Injection, USP**
10 mg/mL

DELUTE PRIOR TO IV INFUSION
Sterile
1 mL Ampule

Rx only

 **SANDOZ**
Brookfield, CO 80020

1002717



Section III.

Labeling

A. Current Labeling

Final Printed Labels
ANDA 77-155
Carton: 2 mL (10 mg/mL) ampoule

NDC 0781-3005-92
Fenoldopam Mesylate Injection, USP

Broomfield, CO 80020

20 mg/2 mL
(10 mg/mL)




Manufactured in Canada by
Sandoz Canada Inc.
Distributed by
Laf Pharmaceutics, Inc.
an affiliate of Sandoz Inc.

Fenoldopam Mesylate Injection, USP
20 mg/2 mL (10 mg/mL)

Broomfield, CO 80020

Fenoldopam Mesylate Injection, USP
20 mg/2 mL (10 mg/mL)

Usual Dosage: See package insert.
Each mL contains: citric acid 3.44 mg, fenoldopam mesylate equivalent to fenoldopam 10 mg, propylene glycol 518 mg, sodium citrate dihydrate 0.61 mg, sodium metabisulfite 1 mg, and water for injection; pH range of 2.8 to 3.9.
Store at 2° to 30°C.
Warning: Dilute before administering. Inspect visually for particulate matter.

NDC 0781-3005-92

Fenoldopam Mesylate Injection, USP
20 mg/2 mL
(10 mg/mL)

DILUTE PRIOR TO IV INFUSION
Sterile
2 mL Ampule

Rx only

 **SANDOZ**
Broomfield, CO 80020

1002720



Section III.

Labeling

A. Current Labeling

**Final Printed Labels
ANDA 77-155
Vials**

A SANDOZ
Kew-Ford, CO 80045
Fenoldopam Mesylate
Injection, USP
10 mg/mL 1 mL
DILUTE PRIOR TO
USE
Sterile
For use only
Manufactured in Canada
Distributed by Sandoz, Inc.
an affiliate of Sandoz Inc.
USP
NDA
1002718

(01)10307813005718

A SANDOZ
Kew-Ford, CO 80045
Fenoldopam Mesylate
Injection, USP
20 mg/2 mL 2 mL
10 mg/mL
DILUTE PRIOR TO
USE
Sterile - For use only
Manufactured in Canada
Distributed by Sandoz, Inc.
an affiliate of Sandoz Inc.
USP
NDA
1002718

(01)10307813005823

Section III.

Labeling

A. Current Labeling

Final Printed Labels

Package Insert



PACKAGE INSERT

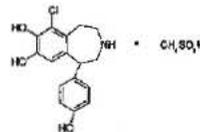
Fenoldopam Mesylate Injection, USP

10 mg/mL

Rx ONLY

DESCRIPTION

Fenoldopam Mesylate Injection, USP is a dopamine D₁-like receptor agonist. The product is formulated as a solution to be diluted for intravenous infusion. Chemically it is 6-chloro-2,3,4,5-tetrahydro-1-(4-hydroxyphenyl)-[1H]-3-benzazepine-7,8-diol methanesulfonate with the following structure:



fenoldopam mesylate

Fenoldopam mesylate is a white to off-white powder with a molecular weight of 401.87 and a molecular formula of C₁₇H₂₀ClNO₆S. It is sparingly soluble in water, ethanol and methanol, and is soluble in propylene glycol.

Ampules: Each mL contains: citric acid 3.44 mg, fenoldopam mesylate equivalent to fenoldopam 10 mg, propylene glycol 518 mg, sodium citrate dihydrate 0.61 mg, sodium metabisulfite 1 mg, and water for injection.

CLINICAL PHARMACOLOGY

Mechanism of Action

Fenoldopam is a rapid-acting vasodilator. It is an agonist for D₁-like dopamine receptors and binds with moderate affinity to α₂-adrenoceptors. It has no significant affinity for D₂-like receptors, α₁ and β adrenoceptors, 5HT₁ and 5HT₂ receptors, or muscarinic receptors. Fenoldopam is a racemic mixture with the R-isomer responsible for the biological activity. The R-isomer has approximately 250-fold higher affinity for D₁-like receptors than does the S-isomer. In non-clinical studies, fenoldopam had no agonist effect on presynaptic D₂-like dopamine receptors, or α- or β-adrenoceptors, nor did it affect angiotensin-converting enzyme activity. Fenoldopam may increase norepinephrine plasma concentration.

In animals, fenoldopam has vasodilating effects in coronary, renal, mesenteric and peripheral arteries. All vascular beds, however, do not respond uniformly to fenoldopam. Vasodilating effects have been demonstrated in renal efferent and afferent arterioles.

Pharmacokinetics

Adult Patients:

Fenoldopam, administered as a constant infusion at rates of 0.01 to 1.6 mcg/kg/min, produced steady-state plasma concentrations that were proportional to infusion rates. The elimination half-life was about 5 minutes in mild to moderate hypertensives, with little difference between the R-(active) and S-isomers. Steady state concentrations are attained in about 20 minutes (4 half-lives). The steady state plasma concentrations of fenoldopam, at comparable infusion rates, were similar in normotensive subjects and in patients with mild to moderate hypertension or hypertensive emergencies.

The pharmacokinetics of fenoldopam were not influenced by age, gender, or race in adult patients with a hypertensive emergency. There have been no formal drug-drug interaction studies using intravenous fenoldopam.

Clearance of parent (active) fenoldopam is not altered in patients with end-stage renal disease on continuous ambulatory peritoneal dialysis (CAPD) and is not affected on average, in severe hepatic failure. The effects of hemodialysis on the pharmacokinetics of fenoldopam have not been evaluated.

Pediatric Patients: Information related to the pharmacokinetics of fenoldopam injection in pediatric patients is approved for Abbott Laboratories' fenoldopam drug products. However, due to Abbott's marketing exclusivity rights, this drug product is not labeled for pediatric use.

In radiolabeled studies in rats, no more than 0.005% of fenoldopam crossed the blood-brain barrier.

Excretion and Metabolism

Radiolabeled studies show that about 90% of infused fenoldopam is eliminated in urine, 10% in feces. Elimination is largely by conjugation, without participation of cytochrome P-450 enzymes. The principal routes of conjugation are methylation, glucuronidation, and sulfation. Only 4% of the administered dose is excreted unchanged. Animal data indicate that the metabolites are inactive.

Pharmacodynamics and Clinical Studies

Adult Patients:

In a randomized double-blind, placebo-controlled, 5-group study in 32 patients with mild to moderate essential hypertension (diastolic blood pressure between 95 and 119 mm Hg), and a mean baseline pressure of about 154/98 mm Hg, and heart rate of about 75 bpm, fixed-rate IV infusions of fenoldopam produced dose-related reductions in systolic and diastolic blood pressure. Infusions were maintained at a fixed rate for 48 hours. Table 1 shows the results of the study. The onset of response was rapid at all infusion rates, with the 15-minute response representing 50-100% of the one-hour response in all groups. There was some suggestion of partial tolerance at 48 hours in the two higher dose infusions, but a substantial effect persisted through 48 hours. When infusions were stopped, blood pressure gradually returned to pretreatment values with no evidence of rebound. This study suggests that there is no greater response to 0.8 mcg/kg/min than to 0.4 mcg/kg/min.

Table 1
 PHARMACODYNAMIC EFFECTS OF FENOLDOPAM
 IN MILD TO MODERATE ADULT HYPERTENSIVE PATIENTS

Time Point and Mean Change from Time Zero ± SE	Infusion Rate (mcg/kg/min)				
	Placebo n = 7	0.04 n = 7	0.1 n = 7	0.4 n = 5	0.8 n = 6



PACKAGE INSERT

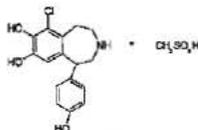
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IN MILD TO MODERATE ADULT HYPERTENSIVE PATIENTS**

Time Point and Mean Change from Time Zero ± SE	Infusion Rate (mcg/kg/min)				
	Placebo n = 7	0.04 n = 7	0.1 n = 7	0.4 n = 5	0.8 n = 6
15 Minutes of Infusion*					
Systolic BP	0 ± 6	-15 ± 6	-19 ± 8	-14 ± 4	-24 ± 6
Diastolic BP	0 ± 2	-5 ± 3	-12 ± 4	-15 ± 3	-20 ± 4
Heart rate	+2 ± 2	+3 ± 2	+5 ± 1	+16 ± 3	+19 ± 3
30 Minutes of Infusion*					
Systolic BP	-6 ± 5	-17 ± 6	-18 ± 6	-14 ± 8	-26 ± 6
Diastolic BP	-6 ± 3	-7 ± 3	-16 ± 4	-14 ± 3	-20 ± 2
Heart rate	+2 ± 2	+3 ± 2	+10 ± 2	+18 ± 3	+23 ± 3
1 Hour of Infusion*					
Systolic BP	-15 ± 4	-22 ± 7	-22 ± 7	-26 ± 9	-22 ± 9
Diastolic BP	-5 ± 3	-9 ± 2	-18 ± 4	-19 ± 4	-21 ± 1
Heart rate	+1 ± 3	+5 ± 2	+12 ± 3	+19 ± 4	+25 ± 4
4 Hours of Infusion*					
Systolic BP	-14 ± 5	-16 ± 9	-31 ± 15	-22 ± 11	-25 ± 7
Diastolic BP	-14 ± 8	-8 ± 4	-19 ± 9	-25 ± 3	-20 ± 1
Heart rate	+5 ± 3	+6 ± 3	+10 ± 4	+21 ± 2	+27 ± 7
24 Hours of Infusion*					

to pretreatment values with no evidence of rebound. This study suggests that there is no greater response to 0.8 mcg/kg/min than to 0.4 mcg/kg/min.

Table 1
PHARMACODYNAMIC EFFECTS OF FENOLDOPAM
IN MILD TO MODERATE ADULT HYPERTENSIVE PATIENTS

Time Point and Mean Change from Time Zero ± SE	Infusion Rate (mcg/kg/min)				
	Placebo n = 7	0.04 n = 7	0.1 n = 7	0.4 n = 5	0.8 n = 6
15 Minutes of Infusion*					
Systolic BP	0 ± 6	-15 ± 6	-19 ± 8	-14 ± 4	-24 ± 6
Diastolic BP	0 ± 2	-5 ± 3	-12 ± 4	-15 ± 3	-20 ± 4
Heart rate	+2 ± 2	+3 ± 2	+5 ± 1	+16 ± 3	+19 ± 3
30 Minutes of Infusion*					
Systolic BP	-6 ± 5	-17 ± 6	-18 ± 6	-14 ± 8	-26 ± 8
Diastolic BP	-6 ± 3	-7 ± 3	-16 ± 4	-14 ± 3	-20 ± 2
Heart rate	+2 ± 2	+3 ± 2	+10 ± 2	+18 ± 3	+23 ± 3
1 Hour of Infusion*					
Systolic BP	-15 ± 4	-22 ± 7	-22 ± 7	-26 ± 9	-22 ± 8
Diastolic BP	-5 ± 3	-9 ± 2	-18 ± 4	-19 ± 4	-21 ± 1
Heart rate	+1 ± 3	+5 ± 2	+12 ± 3	+19 ± 4	+25 ± 4
4 Hours of Infusion*					
Systolic BP	-14 ± 5	-16 ± 9	-31 ± 15	-22 ± 11	-25 ± 7
Diastolic BP	-14 ± 8	-8 ± 4	-19 ± 9	-25 ± 3	-20 ± 1
Heart rate	+5 ± 3	+6 ± 3	+10 ± 4	+21 ± 2	+27 ± 7
24 Hours of Infusion*					
Systolic BP	-20 ± 6	-23 ± 8	-35 ± 7	-22 ± 6	-23 ± 11
Diastolic BP	-11 ± 6	-11 ± 5	-23 ± 10	-22 ± 5	-13 ± 3
Heart rate	+6 ± 3	+5 ± 3	+13 ± 2	+17 ± 4	+15 ± 3
48 Hours of Infusion*					
Systolic BP	-12 ± 8	-31 ± 6	-22 ± 8	-9 ± 6	-14 ± 10
Diastolic BP	-9 ± 5	-10 ± 6	-9 ± 7	-9 ± 2	-8 ± 3
Heart rate	+1 ± 2	0 ± 4	+1 ± 4	+12 ± 3	+6 ± 3

* Mean change from time zero ± S.E.

In a multicenter, randomized, double-blind comparison of four infusion rates, fenoldopam was administered as constant rate infusions of 0.01, 0.03, 0.1 and 0.3 mcg/kg/min for up to 24 hours to 94 adult patients experiencing hypertensive emergencies (defined as diastolic blood pressure ≥ 120 mm Hg with evidence of compromise of end-organ function involving the cardiovascular, renal, cerebral or retinal systems). Infusion rates could be doubled after one hour if clinically indicated. There were dose-related, rapid-onset, decreases in systolic and diastolic blood pressures and increases in heart rate (Table 2).

Table 2
PHARMACODYNAMIC EFFECTS OF FENOLDOPAM
IN HYPERTENSIVE ADULT EMERGENCY PATIENTS

Time Point and Pharmacodynamic Parameters	Infusion Rate mcg/kg/min			
	0.01 n = 26	0.03 n = 24	0.1 n = 22	0.3 n = 23
Pre-Infusion Baseline				
Systolic BP - mean ± SE	210 ± 21	208 ± 26	205 ± 24	211 ± 17
Diastolic BP - mean ± SE	136 ± 16	135 ± 11	133 ± 14	136 ± 15
Heart rate - mean ± SE	87 ± 20	84 ± 14	81 ± 19	80 ± 14
15 Minutes of Infusion*				
Systolic BP	-5 ± 4	-7 ± 4	-16 ± 4	-19 ± 4
Diastolic BP	-5 ± 3	-8 ± 3	-12 ± 2	-21 ± 2
Heart rate	-2 ± 3	+1 ± 1	+2 ± 1	+11 ± 2
30 Minutes of Infusion*				
Systolic BP	-6 ± 4	-11 ± 4	-21 ± 3	-16 ± 4
Diastolic BP	-10 ± 3	-12 ± 3	-17 ± 3	-20 ± 2
Heart rate	-2 ± 3	-1 ± 1	+3 ± 2	+12 ± 3
1 Hour of Infusion*				
Systolic BP	-5 ± 3	-9 ± 4	-19 ± 4	-22 ± 4
Diastolic BP	-8 ± 3	-13 ± 3	-18 ± 2	-23 ± 2
Heart rate	-1 ± 3	0 ± 2	+3 ± 2	+11 ± 3
4 Hours of Infusion*				
Systolic BP	-14 ± 4	-20 ± 5	-23 ± 4	-37 ± 4
Diastolic BP	-12 ± 3	-18 ± 3	-21 ± 3	-29 ± 3
Heart rate	-2 ± 4	0 ± 2	+4 ± 2	+11 ± 2

* Mean change from baseline ± S.E.

Two hundred and thirty six severely hypertensive patients (DBP ≥ 120 mm Hg), with or without end-organ compromise, were randomized to receive in two open-label studies either fenoldopam or nitroprusside. The response rate was 79% (92/117) in the fenoldopam group and 77% (90/119) in the nitroprusside group. Response required a decline in supine diastolic blood pressure to less than 110 mm Hg if the baseline were between 120 and 150 mm Hg, inclusive, or by ≥ 40 mm Hg if the baseline were ≥ 150 mm Hg. Patients were titrated to the desired effect. For fenoldopam, the dose ranged from 0.1 to 1.5 mcg/kg/min; for nitroprusside, the dose ranged from 1.0 to 8.0 mcg/kg/min. As in the study in mild to moderate hypertensives, most of the effect seen at one hour is present at 15 minutes. The additional effect seen after 1 hour occurs in all groups and may not be drug-related (there was no placebo group for evaluation).

Pediatric Patients: Information related to the pharmacodynamics of fenoldopam injection in pediatric patients is approved for Abbott Laboratories' fenoldopam drug products. However, due to Abbott's marketing exclusivity rights, this drug product is not labeled for pediatric use.

INDICATIONS AND USAGE

Adult Patients:

Fenoldopam Mesylate Injection, USP is indicated for the in-hospital, short-term (up to 48 hours) management of severe hypertension when rapid, but quickly reversible, emergency reduction of blood pressure is clinically indicated, including malignant hypertension with deteriorating end-organ function. Transition to oral therapy with another agent can begin at any time after blood pressure is stable during fenoldopam infusion.

Pediatric Patients: Information related to the indicated use of fenoldopam injection in pediatric patients is approved for Abbott Laboratories' fenoldopam drug products. However, due to Abbott's marketing exclusivity rights, this drug product is not labeled for pediatric use.

CONTRAINDICATIONS

None known.

WARNINGS

Use of beta-blockers in conjunction with fenoldopam has not been studied in hypertensive patients and, if possible, concomitant use should be avoided. If the drugs are used together, caution should be exercised because unexpected hypotension could result from beta-blocker inhibition of the reflex response to fenoldopam.

Contains sodium metabisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown.

Two hundred and thirty six severely hypertensive patients (DBP \geq 120 mm Hg), with or without end-organ compromise, were randomized to receive in two open-label studies either fenoldopam or nitroprusside. The response rate was 79% (92/117) in the fenoldopam group and 77% (90/119) in the nitroprusside group. Response required a decline in supine diastolic blood pressure to less than 110 mmHg if the baseline were between 120 and 150 mm Hg, inclusive, or by \geq 40 mm Hg if the baseline were \geq 150 mm Hg. Patients were titrated to the desired effect. For fenoldopam, the dose ranged from 0.1 to 1.5 mcg/kg/min; for nitroprusside, the dose ranged from 1.0 to 8.0 mcg/kg/min. As in the study in mild to moderate hypertensives, most of the effect seen at one hour is present at 15 minutes. The additional effect seen after 1 hour occurs in all groups and may not be drug-related (there was no placebo group for evaluation).

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Contains sodium metabisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

PRECAUTIONS

Intraocular Pressure: In a clinical study of 12 patients with open-angle glaucoma or ocular hypertension (mean baseline intraocular pressure was 29.2 mm Hg with a range of 22.0 - 33.0 mm Hg), infusion of fenoldopam at escalating doses ranging from 0.05 - 0.5 mcg/kg/min over a 3.5 hour period caused a dose-dependent increase in intraocular pressure (IOP). At the peak effect, the intraocular pressure was raised by a mean of 6.5 mm Hg (range -2.0 to +8.5 mm Hg, corrected for placebo effect). Upon discontinuation of the fenoldopam infusion, the IOP returned to baseline values within 2 hours. Fenoldopam Mesylate Injection, USP administration to patients with glaucoma or intraocular hypertension should be undertaken with caution.

Tachycardia: Fenoldopam causes a dose-related tachycardia (Table 1 and Table 2), particularly with infusion rates above 0.1 mcg/kg/min. Tachycardia in adults diminishes over time but remains substantial at higher doses. Tachycardia in pediatric patients at doses $>$ 0.8 mcg/kg/min persists at least for 4 hours.

Hypotension: Fenoldopam may occasionally produce symptomatic hypotension and close monitoring of blood pressure during administration is essential. (See ADVERSE REACTIONS). It is particularly important to avoid systemic hypotension when administering the drug to patients who have sustained an acute cerebral infarction or hemorrhage.

In pediatric patients, fenoldopam was only administered to patients with an indwelling intra-arterial line.

Hypokalemia: Decreases in serum potassium occasionally to values below 3.0 meq/L were observed after less than 8 hours of fenoldopam infusion. It is not clear if the hypokalemia reflects a pressure natriuresis with enhanced potassium-sodium exchange or a direct drug effect. During clinical trials, electrolytes were monitored at intervals of 6 hours. Hypokalemia was treated with either oral or intravenous potassium supplementation. Patient management should include appropriate attention to serum electrolytes.

Intracranial Pressure: The effect of fenoldopam in the presence of increased intracranial pressure has not been studied.

Drug Interactions with Beta-Blockers: Concomitant use of fenoldopam with beta-blockers should be avoided. If the drugs are used together, caution should be exercised because unexpected hypotension could result from beta-blocker inhibition of the sympathetic reflex response to fenoldopam.

Drug Interactions: General: Although there have been no formal interaction studies, intravenous fenoldopam has been administered safely with drugs such as digitalis and sublingual nitroglycerin. There is limited experience with concomitant antihypertensive agents such as beta-blockers, alpha-blockers, calcium channel-blockers, ACE inhibitors, and diuretics (both thiazide-like and loop).

Carcinogenesis, Mutagenesis, Impairment of Fertility: In a 24-month study, mice treated orally with fenoldopam at 12.5, 25, or 50 mg/kg/day, reduced to 25 mg/kg/day on day 209 of study, showed no increase above controls in the incidence of neoplasms. Female mice in the highest dose group had an increased incidence and degree of severity of a fibro-osseous lesion of the sternum compared with control or low-dose animals. Compared to controls, female mice in the middle- and upper-dose groups had a higher incidence and degree of severity of chronic nephritis. These pathologic lesions were not seen in male mice treated with fenoldopam.

In a 24-month study, rats treated orally with fenoldopam at 5, 10 or 20 mg/kg/day, with the mid- and high-dose groups increased to 15 or 25 mg/kg/day, respectively, on day 372 of the study, showed no increase above controls in the incidence or type of neoplasms. Compared with the controls, rats in the mid- and high-dose groups had a higher incidence of hyperplasia of collecting duct epithelium at the tip of the renal papilla.

Fenoldopam did not induce bacterial gene mutation in the Ames test or mammalian gene mutation in the Chinese hamster ovary (CHO) cell assay. In the *in vitro* chromosomal aberration assay with CHO cells, fenoldopam was associated with statistically significant and dose-dependent increases in chromosomal aberrations, and in the proportion of aberrant metaphases. However, no chromosomal damage was seen in the *in vivo* mice micronucleus or bone marrow assays. The data support the conclusion that fenoldopam is not genotoxic or clastogenic.

Oral fertility and general reproduction performance studies in male and female rats at 12.5, 37.5 or 75 mg/kg/day revealed no impairment of fertility or reproduction performance due to fenoldopam.

Pregnancy: Teratogenic Effects: Pregnancy Category B. Oral reproduction studies have been performed in rats and rabbits at doses of 12.5 to 200 mg/kg/day and 6.25 to 25 mg/kg/day, respectively. Studies have revealed maternal toxicity at the highest doses tested but no evidence of impaired fertility or harm to the fetus due to fenoldopam. However, there are no adequate and well-controlled studies in pregnant women. Since animal reproduction studies are not always predictive of human response, fenoldopam should be used in pregnancy only if clearly needed.

Nursing Mothers: Fenoldopam is excreted in milk in rats. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when fenoldopam is administered to a nursing woman.

Pediatric Use: Clinical study information related to the safety and effectiveness of fenoldopam injection in pediatric patients ages < 1 month to 12 years old is approved for Abbott Laboratories' fenoldopam drug products. However, due to Abbott's marketing exclusivity rights, this drug product is not labeled for pediatric use.

Geriatric Use: Clinical studies of fenoldopam did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

ADVERSE REACTIONS

Adult Patients:

Fenoldopam causes a dose-related fall in blood pressure and increase in heart rate (see PRECAUTIONS, Tachycardia, and Hypotension). In controlled clinical studies of severe hypertension in patients with end-organ damage, 3% (4/137) of patients withdrew because of excessive falls in blood pressure. Increased heart rate could, in theory, lead to ischemic cardiac events or worsened heart failure, although these events have not been observed. The most common events reported as associated with fenoldopam use are headache, cutaneous dilation (flushing), nausea, and hypotension, each reported in more than 5% of patients.

Adverse reactions in controlled trials in adult hypertension

Adverse events occurring more than once in any dosing group (once if potentially important or plausibly drug-related) in the fixed-dose constant-infusion studies are presented in the following table by infusion-rate group. There was no clear dose relationship, except possibly for headache, nausea, flushing.

Table 3
ADVERSE EVENTS* FROM FIXED-DOSE INFUSION
STUDIES BY DOSE GROUP

Body System	Event	Fenoldopam Doses (mcg/kg/min)					
		Placebo (n = 7)	0.01 (n = 26)	0.03 - 0.04 (n = 31)	0.1 (n = 28)	0.3 - 0.4 (n = 29)	0.6 - 0.8 (n = 11)
Body, General	Headache	1	5	4	7	8	6
	Injection site reaction	0	1	3	0	3	2
Cardiovascular	ST-T abnormalities (primarily T-wave inversion)	0	2	4	0	1	0
	Flushing	0	0	0	0	1	3
	Hypotension**	0	0	0	2	0	2
	Postural hypotension	0	2	0	0	0	0
	Tachycardia**	0	0	0	0	0	2
Digestive	Nausea	0	3	0	3	5	4
	Vomiting	0	2	0	2	1	2
	Abdominal pain/Fullness	0	2	0	0	2	1
	Constipation	0	0	0	0	0	2
	Diarrhea	0	0	0	0	2	0
Metabolic and Nutritional	Increased creatinine**	0	0	2	0	0	0
	Hypokalemia**	0	2	2	0	1	0
Nervous	Nervousness/Anxiety	0	0	1	0	0	2
	Insomnia	0	2	0	0	0	0
	Dizziness	0	1	1	2	2	0
Respiratory	Nasal congestion	0	0	0	0	0	2
Skin and Appendages	Sweating	0	0	0	1	1	2
Urogenital	Urinary tract infection	0	2	0	1	0	0
Musculoskeletal	Back pain	0	1	0	1	2	2

* Includes events reported by 2 or more patients receiving fenoldopam treatment across all dose groups.

** Investigator defined; no protocol definition.

Adverse effects in overall data base

The adverse event incidences listed below are based on observations of over 1,000 fenoldopam treated adult patients and not listed in Table 3 above.

Events reported with a frequency between 0.5 to 5% in patients treated with IV fenoldopam

Cardiovascular: extrasystoles, palpitations, bradycardia, heart failure, ischemic heart disease, myocardial infarction, angina pectoris

Metabolic: elevated BUN, elevated serum glucose, elevated transaminase, elevated LDH

General Body: non-specific chest pain, pyrexia

Hematologic/Lymphatic: leukocytosis, bleeding

Respiratory: dyspnea, upper respiratory disorder

Genitourinary: oliguria

Musculoskeletal: limb cramp

Pediatric Patients: Information relating to treatment-emergent adverse events is approved for Abbott Laboratories' fenoldopam injection drug products. However, due to Abbott's marketing exclusivity rights, this drug product is not labeled for pediatric use.

ANIMAL TOXICOLOGY

Unusual toxicologic findings (arterial lesions in the rat) with fenoldopam are summarized below. These findings have not been observed in mice or dogs. No evidence of a similar lesion in humans has been observed.

Arterial lesions characterized by medial necrosis and hemorrhage have been seen in renal and splanchnic arteries of rats given fenoldopam mesylate by continuous intravenous infusion at doses of 1 to 100 mcg/kg/min for 24 hours. The incidence of these lesions is dose related. Arterial lesions morphologically identical to those observed with fenoldopam have been reported in rats infused with dopamine. Data suggest that the mechanism for this injury involves activation of D₁-like dopaminergic receptors. Such lesions have not been seen in dogs given doses up to 100 mcg/kg/min by continuous intravenous infusion for 24 hours, nor were they seen in dogs infused at the same dose for 6 hours daily for 24 days. The clinical significance of this finding is not known.

Oral administration of fenoldopam doses of 10 to 15 mg/kg/day or 20 to 25 mg/kg/day to rats for 24 months induced a higher incidence of polyarteritis nodosa compared to controls. Such lesions were not seen in rats given 5 mg/kg/day of fenoldopam or in mice given the drug at doses up to 50 mg/kg/day for 24 months.

OVERDOSAGE

Intentional fenoldopam overdosage has not been reported. The most likely reaction would be excessive hypotension which should be treated with drug discontinuation and appropriate supportive measures.

DOSAGE AND ADMINISTRATION

Adult Patients:

The optimal magnitude and rate of blood pressure reduction in acutely hypertensive patients have not been rigorously determined, but, in general, both delay and too rapid decreases appear undesirable in sick patients. An initial Fenoldopam Mesylate Injection, USP dose may be chosen from Tables 1 and 2 in the Clinical Pharmacology Section that produces the desired magnitude and rate of blood pressure reduction in a given clinical situation. Doses below 0.1 mcg/kg/min have very modest effects and appear only marginally useful in this

Concomitantly, observe
Musculoskeletal: limb cramp

Pediatric Patients: Information relating to treatment-emergent adverse events is approved for Abbott Laboratories' fenoldopam injection drug products. However, due to Abbott's marketing exclusivity rights, this drug product is not labeled for pediatric use.

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Use of a calibrated, mechanical infusion pump is recommended for proper control of infusion rate during Fenoldopam Mesylate Injection, USP infusion. In clinical trials, fenoldopam treatment was safely performed without the need for intra-arterial blood pressure monitoring; blood pressure and heart rate were monitored at frequent intervals, typically every 15 minutes. Frequent blood pressure monitoring is recommended.

The Fenoldopam Mesylate Injection, USP infusion can be abruptly discontinued or gradually tapered prior to discontinuation. Oral antihypertensive agents can be added during Fenoldopam Mesylate Injection, USP infusion or following its discontinuation. Patients in controlled clinical trials have received intravenous fenoldopam for as long as 48 hours.

PREPARATION OF INFUSION SOLUTION

WARNING: CONTENTS OF AMPULES MUST BE DILUTED BEFORE INFUSION. EACH AMPULE IS FOR SINGLE USE ONLY.

Dilution:

Adult Patients:

The Fenoldopam Mesylate Injection, USP ampule concentrate must be diluted in 0.9% Sodium Chloride Injection USP or 5% Dextrose Injection USP using the following dilution schedule:

mL of Concentrate (mg of drug)	Added to	Final Concentration
4 mL (40 mg)	1000 mL	40 mcg/mL
2 mL (20 mg)	500 mL	40 mcg/mL
1 mL (10 mg)	250 mL	40 mcg/mL

The drug dose rate must be individualized according to body weight and according to the desired rapidity and extent of pharmacodynamic effect. Table 4 provides the calculated infusion volume in mL/min for a range of drug doses and body weights. The infusion should be administered using a calibrated mechanical infusion pump that can accurately and reliably deliver the desired infusion rate.

Infusion rate:

Table 4
FENOLDOPAM ADULT INFUSION RATES (mL/hour)
DRUG DOSAGE FOR ADULTS > 40 kg, USING 40 mcg/mL CONCENTRATION
NOTE: CONCENTRATION IS DIFFERENT FROM PEDIATRIC PATIENTS, SEE BELOW: PEDIATRIC PATIENTS

Body Weight (kg)	Infusion Rate				
	0.025 mcg/kg/min	0.05 mcg/kg/min	0.1 mcg/kg/min	0.2 mcg/kg/min	0.3 mcg/kg/min
Infusion Rates (mL/hour) of 40 mcg/mL solution					
40	1.5	3	6	12	18
50	1.9	3.8	7.5	15	22.5
60	2.3	4.5	9	18	27
70	2.6	5.3	10.5	21	31.5
80	3	6	12	24	36
90	3.4	6.8	13.5	27	40.5
100	3.8	7.5	15	30	45
110	4.1	8.3	16.5	33	49.5
120	4.5	9	18	36	54
130	4.9	9.8	19.5	39	58.5
140	5.3	10.5	21	42	63
150	5.6	11.3	22.5	45	67.5

Table 4 (continuation)
FENOLDOPAM ADULT INFUSION RATES (mL/hour)
DRUG DOSAGE FOR ADULTS > 40 kg, USING 40 mcg/mL CONCENTRATION
NOTE: CONCENTRATION IS DIFFERENT FROM PEDIATRIC PATIENTS, SEE BELOW: PEDIATRIC PATIENTS

Body Weight (kg)	Infusion Rate					
	0.5 mcg/kg/min	0.8 mcg/kg/min	1 mcg/kg/min	1.2 mcg/kg/min	1.4 mcg/kg/min	1.6 mcg/kg/min
Infusion Rates (mL/hour) of 40 mcg/mL solution						
40	30	48	60	72	84	96
50	37.5	60	75	90	105	120
60	45	72	90	108	126	144
70	52.5	84	105	126	147	168
80	60	96	120	144	168	192
90	67.5	108	135	162	189	216
100	75	120	150	180	210	240
110	82.5	132	165	198	231	264
120	90	144	180	216	252	288

Table 4

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70	2.6	5.3	10.5	21	31.5
80	3	6	12	24	36
90	3.4	6.8	13.5	27	40.5
100	3.8	7.6	15	30	45
110	4.1	8.3	16.5	33	49.5
120	4.5	9	18	36	54
130	4.9	9.8	19.5	39	58.5
140	5.3	10.5	21	42	63
150	5.6	11.3	22.5	45	67.5

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NOTE: CONCENTRATION IS DIFFERENT FROM PEDIATRIC PATIENTS, SEE BELOW: PEDIATRIC PATIENTS

Body Weight (kg)	Infusion Rate					
	0.5 mcg/kg/min	0.8 mcg/kg/min	1 mcg/kg/min	1.2 mcg/kg/min	1.4 mcg/kg/min	1.6 mcg/kg/min
	Infusion Rates (mL/hour) of 40 mcg/mL solution					
40	30	48	60	72	84	96
50	37.5	60	75	90	105	120
60	45	72	90	108	126	144
70	52.5	84	105	126	147	168
80	60	96	120	144	168	192
90	67.5	108	135	162	189	216
100	75	120	150	180	210	240
110	82.5	132	165	198	231	264
120	90	144	180	216	252	288
130	97.5	156	195	234	273	312
140	105	168	210	252	294	336
150	112.5	180	225	270	315	360

The diluted solution is stable under normal ambient light and temperature conditions for at least 24 hours. Diluted solution that is not used within 24 hours of preparation should be discarded. Parenteral products should be inspected visually. If particulate matter or cloudiness is observed, the drug should be discarded.

Pediatric Patients: Information related to the dosing of fenoldopam injection in pediatric patients is approved for Abbott Laboratories' fenoldopam drug products. However, due to Abbott's marketing exclusivity rights, this drug product is not labeled for pediatric use.

HOW SUPPLIED

NDC - 0781-3005-71 - 1 mL (10 mg/mL), Single-dose ampule, boxes of 1.

NDC - 0781-3005-92 - 2 mL (10 mg/mL), Single-dose ampule, boxes of 1.

Store at 2° to 30°C.



Broomfield, CO 80020

Manufactured in Canada by Sandoz Canada Inc.
 Distributed by Lek Pharmaceuticals, Inc.
 an affiliate of Sandoz Inc.

February 2005

01002719

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 77155

LABELING REVIEWS

APPROVAL SUMMARY
REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 77-155 Date of Submission: January 13, 2005
 Applicant's Name: Sabex 2002 Inc.
 Established Name: Fenoldopam Mesylate Injection USP, 10 mg/mL

APPROVAL SUMMARY

1. Do you have 12 Final Printed Labels and Labeling? Yes

2. CONTAINER – 1 mL single-dose vials

Satisfactory in final print as of the January 13, 2005 submission

\\CDSESUBOGD1\N77155\N 000\2005-01-13\fenoldopam1mLcontainer20050110.pdf

3. CONTAINER – 2 mL single-dose vials

Satisfactory in final print as of the January 13, 2005 submission

\\CDSESUBOGD1\N77155\N 000\2005-01-13\fenoldopam2mLcontainer20050110.pdf

4. CARTON – 1 mL single-dose

Satisfactory in final print as of the January 13, 2005 submission

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5. CARTON – 2 mL single-dose

Satisfactory in final print as of the January 13, 2005 submission

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6. PACKAGE INSERT

Satisfactory in final print as of the January 13, 2005 submission

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7. Revisions needed post-approval: None

8. Patent Data:

Patent Data – NDA 19-922

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
N/A	N/A	None	There are no unexpired patents for this product in the Orange Book Database.	N/A	None

Exclusivity Data– NDA 19-922

Code	Reference	Expiration	Labeling Impact
I-422	INDICATED FOR THE IN-HOSPITAL SHORT-TERM (UP TO 4 HOURS) REDUCTION IN BLOOD PRESSURE IN PEDIATRIC PATIENTS	4/1/07	Carved Out and substituted with Pediatric Division/New Drug Division and OGD recommended statements

BASIS OF APPROVAL:

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Corloпам® Injection

NDA Number: 19-922

NDA Drug Name: Corloпам® Injection

NDA Firm: Abbott Laboratories; N 19-922/SE-005; Approved April 1, 2004

Date of Approval of NDA Insert and supplement: Approved April 1, 2004; N 19-922/SE-005

Has this been verified by the MIS system for the NDA? Yes

Was this approval based upon an OGD labeling guidance? No

Basis of Approval for the Container Labels: Most recently approved labeling of the reference listed drug, Corloпам® Injection.

FOR THE RECORD:

1. The labeling submitted by the firm was based on the most recently approved labeling for this drug product. Labeling was recently approved on April 1, 2004 for the RLD. Used recently approved insert and container/carton labeling for ANDA 76-582 (fenoldopam injection) produced by Bedford Labs for guidance.

2. Patent/ Exclusivities:

Patent Data – NDA 19-922

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
		None	There are no unexpired patents for this product in the Orange Book Database.	N/A	None

Exclusivity Data– NDA 19-922

Code	Reference	Expiration	Labeling Impact
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3. Storage/Dispensing Conditions:

NDA: Store at 2° to 30°C.

ANDA: Store at 2° to 30°C.

(b) (4)

4. Product Line:

The innovator markets their product in two ampule sizes. 1 mL and 2 mL ampules utilizing the concentration of 10mg/mL.

The applicant proposes to market their product in 1 mL and 2 mL ampules utilizing the 10 mg/mL concentration as well.

5. Inactive Ingredients:

The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the **statement of components appearing on page 01-003, Vol. A. 1.1.**

6. Container/Closure

Containers: Type 1 glass container

Closure: Ampule

7. All manufacturing will be done by (b) (4) (See pg.01 001) in vol. A. 1.1)

Date of Review: 1/24/05

Date of Submission: 1/13/05

Primary Reviewer: Jim Barlow

Date: 1/14/05

Team Leader: John Grace

Date: 1/26/05

cc:

ANDA: 77-155
DUP/DIVISION FILE
HFD-613/JBarlow/JGrace (no cc)
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Review

**REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH**

ANDA Number: 77-155
Date of Submission: November 19, 2004
Applicant's Name: Sabex 2002 Inc.
Established Name: Fenoldopam Mesylate Injection USP, 10 mg/mL

Labeling Deficiencies:

1. **CONTAINER – 1 mL and 2 mL single-dose ampules**
Satisfactory in **draft** as of the November 2, 2004 submission.
2. **CARTON**
Satisfactory in **draft** as of the November 2, 2004 submission.
3. **PACKAGE INSERT**
Satisfactory in **draft** as of the November 19, 2004 submission.

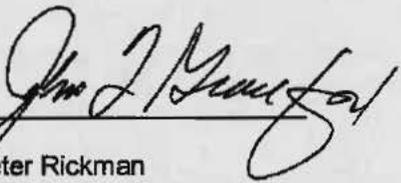
Please prepare and submit final printed labels and labeling in accord with the electronic labeling rule published December 11, 2003, (68 FR 69009) that requires submission of labeling content in electronic format effective June 8, 2004. For additional information, consult the following guidance for industry regarding electronic submissions: Providing Regulatory Submissions in Electronic Format – ANDAs (Issued 6/2002)

(<http://www.fda.gov/cder/guidance/5004fni.htm>)

The guidance specifies labeling to be submitted in pdf format. To assist in our review, we request that labeling also be submitted in MS Word format.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. We suggest that you routinely monitor the following website for any approved changes- <http://www.fda.gov/cder/cdernew/listserv.html> or <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>

To facilitate review of your next submission, and in accordance with 21CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.



Wm. Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

FOR THE RECORD:

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(b) (4)

4. Product Line:

The innovator markets their product in two ampule sizes. 1 mL and 2 mL ampules utilizing the concentration of 10mg/mL.

The applicant proposes to market their product in 1 mL and 2 mL ampules utilizing the 10 mg/mL concentration as well.

5. Inactive Ingredients:

The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the **statement of components appearing on page 01-003, Vol. A. 1.1.**

6. Container/Closure

Containers: Type 1 glass container

Closure: Ampule

7. All manufacturing will be done by (b) (4) (See pg.01 001) in vol. A. 1.1

Date of Review: 11/29/04
 Primary Reviewer: Jim Barlow

Date of Submission: 11/19/04
 Date: 11/29/07

Team Leader: John Grace

Date: 11/29/07

cc:

ANDA: 77-155
 DUP/DIVISION FILE
 HFD-613/JBarlow/JGrace (no cc)
 V:\FIRMSNZ\SABEX\LTRS&REV\77155na3.1.doc
 Review

**REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH**

ANDA Number: 77-155
Date of Submission: November 2, 2004
Applicant's Name: Sabex 2002 Inc.
Established Name: Fenoldopam Mesylate Injection USP, 10 mg/mL

Labeling Deficiencies:

1. **CONTAINER – 1 mL and 2 mL single-dose ampules**
Satisfactory in draft as of the November 2, 2004 submission.
2. **CARTON**
Satisfactory in draft as of the November 2, 2004 submission.
3. **PACKAGE INSERT**
DOSAGE AND ADMINISTRATION -
Table 4: Title – Revise as follows – Delete space between “See Below” and “Pediatric Patients”.

**FENOLDOPAM ADULT INFUSION RATES (mL/hour) DRUG DOSAGE FOR ADULTS > 40 KG,
USING 40MCG/ML CONCENTRATION**

**NOTE: CONCENTRATION IS DIFFERENT FROM PEDIATRIC PATIENTS, SEE BELOW:
PEDIATRIC PATIENTS**

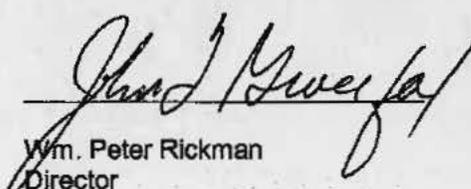
Please revise your labels and labeling, as instructed above, and submit final printed labels and labeling in accord with the electronic labeling rule published December 11, 2003, (68 FR 69009) that requires submission of labeling content in electronic format effective June 8, 2004. For additional information, consult the following guidance for industry regarding electronic submissions: Providing Regulatory Submissions in Electronic Format – ANDAs (Issued 6/2002)

(<http://www.fda.gov/cder/guidance/5004fnl.htm>)

The guidance specifies labeling to be submitted in pdf format. To assist in our review, we request that labeling also be submitted in MS Word format.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. We suggest that you routinely monitor the following website for any approved changes- <http://www.fda.gov/cder/cdernew/listserv.html> or <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>

To facilitate review of your next submission, and in accordance with 21CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.


Wm. Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

FOR THE RECORD:

1. The labeling submitted by the firm was based on the most recently approved labeling for this drug product. Labeling was recently approved on April 1, 2004 for the RLD. Used recently approved insert and container/carton labeling for ANDA 76-582 (fenoldopam injection) produced by Bedford Labs for guidance.

2. Patent/ Exclusivities:

Patent Data – NDA 19-922

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
		None	There are no unexpired patents for this product in the Orange Book Database.	N/A	None

Exclusivity Data– NDA 19-922

Code	Reference	Expiration	Labeling Impact
1-422	INDICATED FOR THE IN-HOSPITAL SHORT-TERM (UP TO 4 HOURS) REDUCTION IN BLOOD PRESSURE IN PEDIATRIC PATIENTS	4/1/07	Carved Out and substituted with Pediatric Division/New Drug Division and OGD recommended statements

3. Storage/Dispensing Conditions:

NDA: Store at 2° to 30°C.

ANDA: Store at 2° to 30°C.

(b) (4)

4. Product Line:

The innovator markets their product in two ampule sizes. 1 mL and 2 mL ampules utilizing the concentration of 10mg/mL.

The applicant proposes to market their product in 1 mL and 2 mL ampules utilizing the 10 mg/mL concentration as well.

5. Inactive Ingredients:

The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the **statement of components appearing on page 01-003, Vol. A. 1.1.**

6. Container/Closure

Containers: Type 1 glass container

Closure: Ampule

7. All manufacturing will be done by (b) (4) (See pg.01 001) in vol. A. 1.1

Date of Review: 11/12/04

Date of Submission: 11/2/04

Primary Reviewer: Jim Barlow

Date: *[Signature]*

Team Leader: John Grace

Date: *[Signature]* 11/15/04

cc:

ANDA: 77-155
DUP/DIVISION FILE
HFD-613/JBarlow/JGrace (no cc)
V:\FIRMSNZ\SABEX\LTRS&REV\77155na2.1.doc
Review

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
ANDA 77155

CHEMISTRY REVIEWS

ANDA 77-155

**Fenoldopam Mesylate Injection USP,
10mg (base)/1mL and 20mg (base)/2mL**

Sabex 2002, Inc.

**Yusuf Amin
Chemistry Division I**



Table of Contents

Table of Contents	2
Chemistry Review Data Sheet	3
The Executive Summary	7
I. Recommendations.....	7
A. Recommendation and Conclusion on Approvability	7
B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable	7
II. Summary of Chemistry Assessments.....	7
A. Description of the Drug Product(s) and Drug Substance(s).....	7
B. Description of How the Drug Product is Intended to be Used.....	7
C. Basis for Approvability or Not-Approval Recommendation	7
III. Administrative.....	8
A. Reviewer's Signature.....	8
B. Endorsement Block.....	8
C. CC Block.....	8
Chemistry Assessment	9
Ingredients used for Fenoldopam Mesylate Injection, USP	9

Chemistry Review Data Sheet

1. ANDA # 77-155
2. REVIEW #: 2
3. REVIEW DATE: 16-NOV-2004
4. REVIEWER: Yusuf Amin

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Original	20-MAY-2004
Telephone Amendment	19-JUL-2004

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Amendment (Chemistry)	03-NOV-2004
Amendment (Labeling)	13-JAN-2005
Amendment (Chemistry)	27-JAN-2005
Amendment (Micro)	27-JAN 2005

7. NAME & ADDRESS OF APPLICANT:

Name:	SABEX 2002 Inc.
Address:	145 Jules Leger Street, Boucherville (QC) Canada J4B 7K8
U.S. Agent:	Beth Brannan Sandoz Pharmaceuticals, Inc. 2555 W. Midway Blvd. P.O.Box 446 Broomfield, CO 80038
Telephone:	303-438-4237
Fax:	1-866-301-6408

8. DRUG PRODUCT NAME/CODE/TYPE:

Fenoldopam Mesylate Injection, USP

9. LEGAL BASIS FOR SUBMISSION: FFD & CA

Paragraph II Certification: The basis for submission is the approved listed drug Corlopam® Fenoldopam Mesylate Injection USP, the subject of NDA #19-922 held by Hospira. Sabex certifies that in its opinion and to the best of its knowledge, no unexpired

CHEMISTRY REVIEW

Chemistry Review Data Sheet

Sabex certifies that in its opinion and to the best of its knowledge, the pediatric exclusivity code No. I-422 expiring on April 1st 2007 will not be infringed and there will be no claims on its labeling in regards to this exclusivity (Amendment dated 19-JUL-2004).

10. PHARMACOL. CATEGORY: Short-term management of severe hypertension.

11. DOSAGE FORM: Injection

12. STRENGTH/POTENCY: 10 mg (base)/mL

13. ROUTE OF ADMINISTRATION: Intravenous

14. Rx/OTC DISPENSED: Rx OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

SPOTS product – Form Completed

Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Generic Name: Fenoldopam Mesylate

Chemical Name: 6-chloro-2,3,4,5-tetrahydro-1-(4-hydroxyphenyl)-[1 H]-3-benzazepine-7,8-diol methanesulfonate

Formula: $C_{16}H_{16}ClNO_3 \cdot CH_3SO_3H$

Molecular weight: 401.87

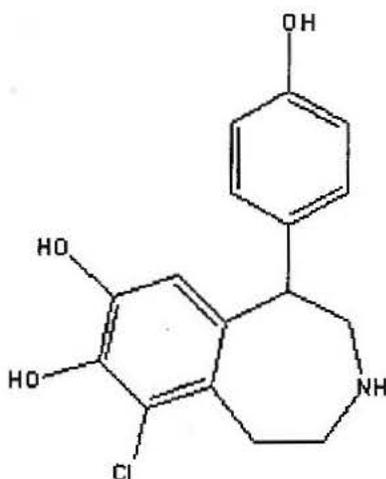
CAS registry number(s): 67227-57-0

Hypertension

Chemical Structure: $C_{16}H_{16}ClNO_3 \cdot CH_3SO_3H$



Chemistry Review Data Sheet



.CH₃SO₃H

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II	(b) (4)	(b) (4)	1	Adequate	11/24/2004	Reviewed by Y.Amin
	III			4			

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

² Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: None

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
Corlopam® Hospira	19-922	RLD



CHEMISTRY REVIEW



Chemistry Review Data Sheet

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	Satisfactory	9-FEB-2005	N. Nath
EES	Satisfactory	27-JAN-2005	S. Adams
Methods Validation	N/A		
Labeling	Satisfactory	26-JAN-2005	J. Barlow
Bioequivalence	Waiver granted	09-NOV-2004	B. Fritsch
EA	Acceptable	11-AUG-2004	Y.Amin
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. Yes No If no, explain reason(s) below:



The Chemistry Review for ANDA 77-155

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

CMC approvable.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

The drug substance used to manufacture of the drug product, Fenoldopam Mesylate Injection 10mg/ml, is a white to off-white powder that is

(b) (4)

(b) (4)

formulated with known compendium excipients to form the drug product.

The drug product is based on the listed drug Corlopan® Fenoldopam Mesylate Injection USP, the subject of NDA #19-922 held by Hospira. The drug is a rapid-acting vasodilator. It is an agonist for D₁-like dopamine receptors and binds with moderate affinity to (alpha)₂ -adrenoreceptors. It has no significant affinity for D₂-like receptors (alpha)₁ and (beta) -adrenoreceptors, 5HT₁ and 5HT₂ receptors or muscarinic receptors. Fenoldopam is a racemic mixture with the R-isomer responsible for the biological activity. The product is formulated as a solution to be diluted for intravenous infusion.

B. Description of How the Drug Product is Intended to be Used

The recommended dose 0.1 µg/kg/ml is administered by continuous intravenous injection with increments of 0.05 µg/kg/ml to 0.1 µg/kg/ml after 15 minutes followed by monitoring of blood pressure. Maximum Daily Dose based on 70 kg patient's weight and highest rate of 1.6 µg/Kg/min, which is $70 \times 1.6 \times 60 = 6,720 \mu\text{g/hr}$ (using 40 µg/mL concentration, 168 mL/Hour is administered). The maximum daily dose will be 161.28 mg/24 hours. (Reference: Packaging inserts).

C. Basis for Approvability or Not-Approval Recommendation

CMC approvable.

Chemistry Review Data Sheet

III. Administrative

A. Reviewer's Signature

Yusuf Amin

B. Endorsement Block

Reviewer:HFD-623/Y.Amin/11/24/2004

Team Leader:HFD-623/A. Mueller/

Project Manager: HFD-617/S. Eng/

F/t: SE

FOR Rev 02/10/05
A. Mueller 2-10-05
2/10/05

C. CC Block: N/A

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Chemistry Review Data Sheet

Controlled Room Temperature Stability Data:

Sabex submitted 9 months controlled room temperature stability data for the drug product packaged in the container/closure system. There are no significant statistical trends in the submitted data as the test results meet the current proposed specifications.

30. MICROBIOLOGY: Satisfactory, N. Nath 2/9/05

The information submitted on sterility is currently under review by our Microbiology Team. Any deficiencies found will be communicated to you under separate cover.

31. SAMPLES AND RESULTS/METHODS VALIDATION STATUS:

The drug substance and the drug product are compendium items, therefore methods validation is not required.

32. LABELING: Satisfactory, 1/26/05, J. Barlow.

33. ESTABLISHMENT INSPECTION: Acceptable, S. Adams 1/27/05

34. BIOEQUIVALENCE: Waiver granted 11/9/2004, B. Fritsch

35. ENVIRONMENTAL IMPACT CONSIDERATIONS/CATEGORICAL EXCLUSION: Satisfactory in review 1

Sabex requests a categorical exclusion from requirement of an environmental assessment statement and certifies compliance of all applicable local, state, and federal environmental regulations (Section 1.2.7, Vol. 1.1).

cc: ANDA # 77-155
ANDA DUP # 77-155
DIV FILE
Field Copy

Endorsements:

Reviewer:HFD-623/Y.Amin/11/24/2004
Team Leader:HFD-623/A. Mueller/
Project Manager: HFD-617/S. Eng/

C. CC Block: N/A

F/T:

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TYPE OF LETTER: CMC APPROVABLE

ANDA 77-155

**Fenoldopam Mesylate Injection USP,
10mg (base)/1mL and 20mg (base)/2mL**

Sabex 2002, Inc.

**Yusuf Amin
Chemistry Division I**



Table of Contents

Table of Contents	2
Chemistry Review Data Sheet.....	3
The Executive Summary.....	7
I. Recommendations.....	7
A. Recommendation and Conclusion on Approvability.....	7
B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable	7
II. Summary of Chemistry Assessments.....	7
A. Description of the Drug Product(s) and Drug Substance(s).....	7
B. Description of How the Drug Product is Intended to be Used	7
C. Basis for Approvability or Not-Approval Recommendation	7
III. Administrative.....	8
A. Reviewer's Signature	8
B. Endorsement Block	8
C. CC Block.....	8
Chemistry Assessment	9
Ingredients used for Fenoldopam Mesylate Injection, USP	9



Chemistry Review Data Sheet

1. ANDA # 77-155
2. REVIEW #: 1
3. REVIEW DATE: 08/10/2004
4. REVIEWER: Yusuf Amin

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
None	

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original	20-MAY-2004
Telephone Amendment	19-JUL-2004

7. NAME & ADDRESS OF APPLICANT:

Name:	SABEX 2002 Inc.
Address:	145 Jules Leger Street, Boucherville (QC) Canada J4B 7K8
U.S. Agent:	George S. Zorich Roundtable Healthcare Partners, 272 E. Deerpath Street, Suite 350, Lake Forest IL 60045
Telephone:	(847) 739-3296
Fax:	(866) 301-6408

8. DRUG PRODUCT NAME/CODE/TYPE:

Fenoldopam Mesylate Injection, USP

9. LEGAL BASIS FOR SUBMISSION: FFD & CA

Paragraph II Certification: The basis for submission is the approved listed drug Corlopan® Fenoldopam Mesylate Injection USP, the subject of NDA #19-922 held by Hospira. Sabex certifies that in its opinion and to the best of its knowledge, no unexpired patents exist for Corlopan® Fenoldopam Mesylate Injection USP, the subject of NDA #19-922 held by Hospira.

**Chemistry Review Data Sheet**

Sabex certifies that in its opinion and to the best of its knowledge, the pediatric exclusivity code No. I-422 expiring on April 1st 2007 will not be infringed and there will be no claims on its labeling in regards to this exclusivity (Amendment dated 19-JUL-2004).

10. PHARMACOL. CATEGORY: Short-term management of severe hypertension.
11. DOSAGE FORM: Injection
12. STRENGTH/POTENCY: 10 mg (base)/mL
13. ROUTE OF ADMINISTRATION: Intravenous
14. Rx/OTC DISPENSED: Rx OTC
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
 SPOTS product – Form Completed
 Not a SPOTS product
16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Generic Name: Fenoldopam Mesylate

Chemical Name: 6-chloro-2,3,4,5-tetrahydro-1-(4-hydroxyphenyl)-[1 H]-3-benzazepine-7,8-diol methanesulfonate

Formula: $C_{16}H_{16}ClNO_3 \cdot CH_3SO_3H$

Molecular weight: 401.87

CAS registry number(s): 67227-57-0

Hypertension



CHEMISTRY REVIEW



Chemistry Review Data Sheet

Chemical Structure:



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II		(b) (4)	1	Inadequate	08/24/2004	Reviewed by Y.Amin
	III			4			

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

² Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: None

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
Corlopam® Hospira	19-922	RLD



CHEMISTRY REVIEW



Chemistry Review Data Sheet

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	Pending		
EES	Pending		
Methods Validation	N/A		
Labeling	Pending		
Bioequivalence	Pending		
EA	Acceptable	11-AUG-2004	Y.Amin
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. Yes No If no, explain reason(s) below:



The Chemistry Review for ANDA 77-155

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The chemistry section is deficient in areas of manufacturing and controls and is therefore recommended for “not-approvable”.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

The drug substance used to manufacture of the drug product, Fenoldopam Mesylate Injection 10mg/ml, is a white to off-white powder that is

(b) (4)

(b) (4)

formulated with known compendium excipients to form the drug product.

A. The drug product is based on the listed drug Corlopam® Fenoldopam Mesylate Injection USP, the subject of NDA #19-922 held by Hospira. The drug is a rapid-acting vasodilator. It is an agonist for D₁-like dopamine receptors and binds with moderate affinity to (alpha)₂ –adrenoreceptors. It has no significant affinity for D₂-like receptors (alpha)₁ and (beta) –adrenoreceptors, 5HT₁ and 5HT₂ receptors or muscarinic receptors. Fenoldopam is a racemic mixture with the R-isomer responsible for the biological activity. The product is formulated as a solution to be diluted for intravenous infusion.

B. Description of How the Drug Product is Intended to be Used

The recommended dose 0.1 µg/kg/ml is administered by continuous intravenous injection with increments of 0.05 µg/kg/ml to 0.1 µg/kg/ml after 15 minutes followed by monitoring of blood pressure.

C. Basis for Approvability or Not-Approval Recommendation

The “not-approvable” recommendation for chemistry is based on the following issues:

- The Drug Master File # (b) (4) is deficient.



CHEMISTRY REVIEW



Chemistry Review Data Sheet

- Some issues in the controls of the drug product both for release and stability that need to be resolved.

III. Administrative

A. Reviewer's Signature

Yusuf Amin

B. Endorsement Block

Reviewer: HFD-623/Y.Amin/8/25/2004

Team Leader: HFD-623/A. Mueller/8/28/04

Project Manager: HFD-617/S. Eng/9/15/04

f/t:ard/9/16/04

Y.Amin - 9/17/04
A. Mueller 9-19-04, 10-21-04
** 9/20/04*

C. CC Block: N/A

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30. MICROBIOLOGY: Pending

The information submitted on sterility is currently under review by our Microbiology Team. Any deficiencies found will be communicated to you under separate cover.

31. SAMPLES AND RESULTS/METHODS VALIDATION STATUS:

The drug substance and the drug product are compendium items, therefore methods validation is not required.

32. LABELING: Pending

33. ESTABLISHMENT INSPECTION: Pending

34. BIOEQUIVALENCE: Pending

The bioequivalence information that you have provided is currently under review. After this review is completed, any deficiencies found will be communicated to you under a separate cover.

35. ENVIRONMENTAL IMPACT CONSIDERATIONS/CATEGORICAL EXCLUSION: Satisfactory

Sabex requests a categorical exclusion from requirement of an environmental assessment statement and certifies compliance of all applicable local, state, and federal environmental regulations (Section 1.2.7, Vol. 1.1).

36. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: #77-155

APPLICANT: Sabex 2002, Inc.

DRUG PRODUCT: Fenoldopam Mesylate Injection USP, 10mg/1mL and 20mg/2mL

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. The DMF # (b) (4) was reviewed and found to be inadequate. Please do not respond until the DMF holder has responded to their deficiencies.

2.

3.

4.

5.

6.

7.

(b) (4)

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. Please provide current room temperature stability data.
2. The labeling information that you have provided is under review . The deficiencies found will be communicated to you under a separate cover.
3. The bioequivalence information that you have provided is currently under review. After this review is completed, any deficiencies found will be communicated to you under a separate cover.

4. The information submitted on sterility is currently under review by our Microbiology team. Any deficiencies found will be communicated to you under a separate cover.

Sincerely yours,

Rashmikant Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA # 77-155
ANDA DUP # 77-155
DIV FILE
Field Copy

Endorsements:

Reviewer:HFD-623/Y.Amin/8/25/2004
Team Leader:HFD-623/A. Mueller/8/28/04
Project Manager: HFD-617/S. Eng/9/15/04

9/17/04
Mueller 10-21-04

C. CC Block: N/A

F/T:ard/9/16/04

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TYPE OF LETTER: NOT APPROVABLE - MINOR

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
ANDA 77155

MICROBIOLOGY REVIEWS

Product Quality Microbiology Review

Review for HFD-620

4 February 2005

ANDA: 77-155

Drug Product Name

Proprietary: None

Non-proprietary: Fenoldopam Mesylate Injection, USP

Drug Product Classification: N/A

Review Number: #2

Subject of this Review

Submission Date: January 27, 2005

Receipt Date: January 28, 2005

Consult Date: N/A

Date Assigned for Review: February 3, 2005

Submission History (for amendments only)

Date(s) of Previous Submission(s): May 20, 2004

(Rec'd May 24, 2004)

Date(s) of Previous Micro Review(s): December 23, 2004

Applicant/Sponsor

Name: Sabex 2002 Inc.,

Address: 145 Jules-Leger Street, Boucherville, (QC), Canada J4B7K8

Representative: Ms. Beth Brannan, Sandoz Pharmaceuticals, Inc.

Telephone: 303-438-4237

Alternate Ms. Louise Fortin, Manager Regulatory Affairs

Telephone: 450- 641-4903, ext. 2169

Name of Reviewer: Nrapendra Nath

Conclusion: The submission is recommended for approval on the basis of sterility assurance.

Product Quality Microbiology Data Sheet

- A.**
1. **TYPE OF SUPPLEMENT:** N/A
 2. **SUPPLEMENT PROVIDES FOR:** N/A
 3. **MANUFACTURING SITE:**

(b) (4)
 4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** 10mg/mL as 1mL in 1mL glass ampoules and 2mL in 2mL glass ampoules; I/V infusion.
 5. **METHOD(S) OF STERILIZATION:**

(b) (4)

(b) (4)
 6. **PHARMACOLOGICAL CATEGORY:** Anti-hypertensive for short-term management of severe hypertension.
- B. SUPPORTING/RELATED DOCUMENTS:** None.
- C. REMARKS:**

(b) (4)

(b) (4)

Executive Summary

I. Recommendations

- A. Recommendation on Approvability –**
The submission is **recommended** for approval on the basis of sterility assurance. Specific comments are provided in the "Product Quality Microbiology Assessment" section.
- B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable – N/A**

II. Summary of Microbiology Assessments

- A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology –**
The subject drug product is manufactured (b) (4)
(b) (4)
- B. Brief Description of Microbiology Deficiencies –**
None.
- C. Assessment of Risk Due to Microbiology Deficiencies –**
N/A.

III. Administrative

- A. Reviewer's Signature** Nrapendra N. 12 2/9/2005
- B. Endorsement Block**
Microbiology Reviewer: Nrapendra Nath, Ph.D.
Microbiology Team Leader: Neal J. Sweeney, Ph.D.
- C. CC Block**
cc:
Original ANDA
Division File
Field Copy
Filename: V:\MICROREV\77-155a1.doc

Neal J. Sweeney
2-9-05

Product Quality Microbiology Review

Review for HFD-620

23 December 2004

ANDA: 77-155

Drug Product Name

Proprietary: None

Non-proprietary: Fenoldopam Mesylate Injection, USP

Drug Product Classification: N/A

Review Number: #1

Subject of this Review

Submission Date: May 20, 2004;

Receipt Date: May 24, 2004

December 16, 2004 (Gratuitous Amendment); Rec'd December 17, 2004

Consult Date: N/A

Date Assigned for Review: November 15, 2004

Submission History (for amendments only)

Date(s) of Previous Submission(s): N/A

Date(s) of Previous Micro Review(s): N/A

Applicant/Sponsor

Name: Sabex 2002 Inc.,

Address: 145 Jules-Leger Street, Boucherville, (QC), Canada J4B7K8

Representative: Ms. Louise Fortin, Manager Regulatory Affairs.

Telephone: 450- 641-4903, ext. 2169

Name of Reviewer: Nrapendra Nath

Conclusion: The submission is **not recommended** for approval on the basis of sterility assurance.

Product Quality Microbiology Data Sheet

- A.**
- 1. TYPE OF SUPPLEMENT:** N/A
 - 2. SUPPLEMENT PROVIDES FOR:** N/A
 - 3. MANUFACTURING SITE:**

(b) (4)
 - 4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** 10mg/mL as 1mL in 1mL glass ampoules and 2mL in 2mL glass ampoules; I/V infusion.
 - 5. METHOD(S) OF STERILIZATION:**

(b) (4)

(b) (4)
 - 6. PHARMACOLOGICAL CATEGORY:** Anti-hypertensive for short-term management of severe hypertension.
- B. SUPPORTING/RELATED DOCUMENTS:** None.
- C. REMARKS:** The subject review used CTD template because the application is presented in this format.

Note to Chemist:

(b) (4)

(d) (4)

Executive Summary

I. Recommendations

- A. Recommendation on Approvability –**
The submission is **not recommended** for approval on the basis of sterility assurance. Specific comments are provided in the "Product Quality Microbiology Assessment" and "List of Microbiology Deficiencies and Comments" sections.
- B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable – N/A**

II. Summary of Microbiology Assessments

- A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology –**
The subject drug product is manufactured (b) (4)
(b) (4)
- B. Brief Description of Microbiology Deficiencies –**
Insufficient documentation of various validation reports and other deficiencies require explanation and documentation.
- C. Assessment of Risk Due to Microbiology Deficiencies –**
Low.

III. Administrative

- A. Reviewer's Signature** Nrapendra Nath 1/6/2005
- B. Endorsement Block**
Microbiology Reviewer: Nrapendra Nath, Ph.D.
Microbiology Team Leader: Neal J. Sweeney, Ph.D.
- C. CC Block**
cc:
Original ANDA
Division File
Field Copy
Filename: V:\MICROREV\77-155.doc

3. LIST OF MICROBIOLOGY DEFICIENCIES AND COMMENTS:

ANDA: 77-155

APPLICANT: Sabex 2002 Inc.

DRUG PRODUCT: Fenoldopam Mesylate Injection, USP

A. Microbiology Deficiencies:

1.

(b) (4)

2.

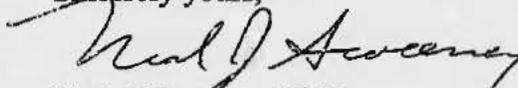
3.

4.

5.

Please clearly identify your amendment to this facsimile as "RESPONSE TO MICROBIOLOGY DEFICIENCIES". The "RESPONSE TO MICROBIOLOGY DEFICIENCIES" should also be noted in your cover page/letter.

Sincerely yours,



Neal J. Sweeney, Ph.D.
Microbiology Team Leader
Office of Generic Drugs
Center for Drug Evaluation and Research

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
ANDA 77155

BIOEQUIVALENCE REVIEWS

DIVISION OF BIOEQUIVALENCE REVIEW

ANDA No.:	77-155
Drug Product Name	Fenoldopam Mesylate Injection USP
Strength	10 mg/mL, 1 mL and 2 mL Ampoules
Applicant Name	Roundtable Healthcare Partners
	U.S. Agent for: Sabex 2002 Inc.
Address	272 E. Deerpath Street, Suite 350, Lake Forest, IL 60045
Submission Date(s)	May 20, 2004
Amendment Date(s)	NA
Reviewer	Beth Fabian Fritsch, R.Ph., MBA
First Generic	No
File Location	V: firmsnz/sabex/ltrs&rev/77155W0504.doc

I. Submission Summary

The test product is qualitatively and quantitatively the same as the reference listed drug. Therefore, Sabex 2002 Inc's Fenoldopam Mesylate Injection USP, 10 mg/mL, 1 mL and 2 mL ampoules is deemed bioequivalent to the reference listed drug Corlopam[®] Injection (Fenoldopam Mesylate Injection USP), 10 mg/mL under 21 CFR 320.22(b)(1).

A. Drug Product Information

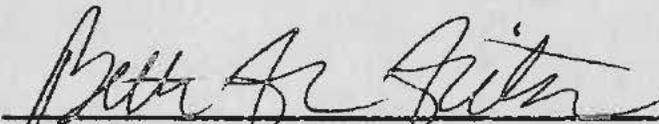
Test Product	Fenoldopam Mesylate Injection USP, 10 mg/mL
Reference Product	Corlopam Injection, 10 mg/mL
RLD Manufacturer	Hospira
NDA No.	19-922
RLD Approval Date	September 23, 1997
Indication	In-hospital, short-term (up to 48 hours) management of severe hypertension when rapid, but quickly reversible, emergency reduction of blood pressure is clinically indicated

B. Formulation

Ingredient	Test	Reference
Fenoldopam Mesylate	10 mg/mL	10 mg/mL
Citric Acid	3.44 mg	3.44 mg
Propylene Glycol	518 mg	518 mg
Sodium Citrate Dihydrate	0.61 mg	0.61 mg
Sodium Metabisulfite	1 mg	1 mg
Water for Injection	q.s. 1 mL	(b) (4)

Recommendations

The Division of Bioequivalence agrees that the information submitted by Sabex 2002 Inc. demonstrates that its test product Fenoldopam Mesylate Injection USP, 10 mg/mL, 1 mL and 2 mL Ampoules falls under the criteria set forth in 21 CFR 320.22(b)(1) of the Bioavailability/ Bioequivalence Regulations. The waiver is granted.



Beth Fabian Fritsch, R.Ph., MBA
Project Manager, Branch IV



Lizzie Sanchez, Pharm.D.
Special Assistant to the Director
Division of Bioequivalence

11/9/04



Dale P. Conner, Pharm. D.
Director, Division of Bioequivalence
Office of Generic Drugs

11/15/04

BIOEQUIVALENCE COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 77-155

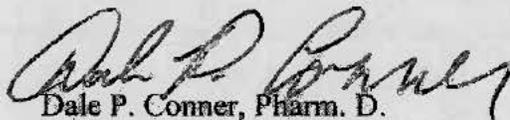
APPLICANT: Sabex 2002 Inc.

DRUG PRODUCT: Fenoldopam Mesylate Injection USP 10 mg/mL, 1 mL and 2 mL Ampoules

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,



Dale P. Conner, Pharm. D.

Director,

Division of Bioequivalence

Office of Generic Drugs

Center for Drug Evaluation and Research

CC: ANDA 77-155
ANDA DUPLICATE
DIVISION FILE

Printed in final on

Endorsements: (Final with Dates)

HFD-655/ B. Fritsch *BFA*

HFD-655/ L. Sanchez

HFD-650/ D. Conner *DC 11/15/01*

BIOEQUIVALENCE - ACCEPTABLE Submission date: May 20, 2004

1. **WAIVER (WAI)**

Strengths: 10 mg/mL,
1 ml and 2 mL
Outcome: AC

Outcome: AC- Acceptable

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
ANDA 77155

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

FAX Cover Sheet – Microbiology Deficiencies Enclosed

Office of Generic Drugs, CDER, FDA

Document Control Room, Metro Park North II

7500 Standish Place, Room 150

Rockville MD 20855-2773 (301-594-0320)



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TO: Louise Fortin	FROM: Mark Anderson
Sabex 2002 inc.	Microbiology Project Manager
PHONE: 450-641-4903 X2169	PHONE: (301) 827-0530
FAX: 1-866-301-6408	FAX: (301) 827-5911

Total number of pages, excluding this cover sheet: 2

Date: January 10, 2005

Microbiology Deficiencies:

Enclosed are the microbiology deficiencies for ANDA 77-155. The submission(s) reviewed was submitted on "December 16, 2004". Please respond to this letter as quickly as possible. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT-RESPONSE TO MICROBIOLOGY DEFICIENCIES should appear prominently in your cover letter.

Should you also have other outstanding deficiencies, for review purposes, please attempt to consolidate your responses into a single submission for this application.

If you have questions, feel free to call me or Bonnie McNeil.

Mark Anderson

3. LIST OF MICROBIOLOGY DEFICIENCIES AND COMMENTS:

ANDA: 77-155

APPLICANT: Sabex 2002 Inc.

DRUG PRODUCT: Fenoldopam Mesylate Injection, USP

A. Microbiology Deficiencies:

1.

2.

3.

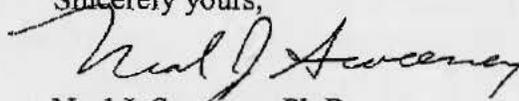
4.

(b) (4)

5.

Please clearly identify your amendment to this facsimile as "RESPONSE TO MICROBIOLOGY DEFICIENCIES". The "RESPONSE TO MICROBIOLOGY DEFICIENCIES" should also be noted in your cover page/letter.

Sincerely yours,



Neal J. Sweeney, Ph.D.
Microbiology Team Leader
Office of Generic Drugs
Center for Drug Evaluation and Research

OGD APPROVAL ROUTING SUMMARY

ANDA # 77-155 Applicant Sabex 2002 Inc.

Drug Penol dopamine Mesylate Injection, ASP Strength(s) 10mg/ml

APPROVAL TENTATIVE APPROVAL SUPPLEMENTAL APPROVAL (NEW STRENGTH) OTHER

REVIEWER:

1. Martin Shimer
Chief, Reg. Support Branch

DRAFT Package

Date 5/12/05
Initials MS

FINAL Package

Date 2/15/05
Initials [Signature]

Contains GDEA certification: Yes No
(required if sub after 6/1/92)

Determ. of Involvement? Yes No
Pediatric Exclusivity System:

Patent/Exclusivity Certification: Yes No

RLD = 19-922
Date Checked Previously granted

If Para. IV Certification- did applicant

Nothing Submitted

Notify patent holder/MDA holder Yes No

Written request issued

Was applicant sued w/in 45 days: Yes No

Study Submitted

Has case been settled: Yes No

Date settled:

Is applicant eligible for 180 day

Generic Drugs Exclusivity for each strength: Yes No

Date of latest Labeling Review/Approval Summary 11/11/2005

Any filing status changes requiring addition Labeling Review: Yes No

Type of Letter:

Comments:

no patent/exclusivities :. original full report pending KABS emailed OC 12/14 for update

2. Project Manager, [Signature] Team [Signature]
Review Support Branch

Date _____ Date _____
Initials _____ Initials _____

Original Rec'd date 5/20/04

EER Status Pending Acceptable OAI

Date Acceptable for Filing 5/27/04

Date of EER Status 1/27/05

Patent Certification (type) T

Date of Office Bio Review 11/15/04

Date Patent/Exclus. expires N/A

Date of Labeling Approv. Sum 1/26/05

Citizens' Petition/Legal Case Yes No

Labeling Acceptable Email Rec'd Yes No

(If YES, attach email from PM to CP coord)

Labeling Acceptable Email filed Yes No

First Generic Yes No

Date of Sterility Assur. App. 2/9/05 Micro

Pharmatizer AP on 11/1/03 76656

Methods Val. Samples Pending Yes No OK

MV Commitment Rcd. from Firm Yes No

Acceptable Bio reviews tabbed Yes No

Modified-release dosage form: Yes No

Suitability Petition/Pediatric Waiver

Interim Dissol. Specs in AP Ltr: Yes

Pediatric Waiver Request Accepted Rejected Pending

Previously reviewed and tentatively approved

Date X

Previously reviewed and CGMP def. /NA Minor is sued

Date X

Comments:

Corlopan INT of

3. David Read (PP IVs Only) Pre-MMA Language included
OGD Regulatory Counsel, Post-MMA Language Included
Comments:

Date _____
Initials _____

NA

4. Div. Dir./Deputy Dir.
Chemistry Div. I II OR III
Comments:

Date 2/11
Initials [Signature]

CMC OK

REVIEWER:

FINAL ACTION

5. Frank Holcombe First Generics Only Date _____
 Assoc. Dir. For Chemistry Initials _____
 Comments: (First generic drug review)
 N/A. Both Pharmforce (ANDA 76-656) and Bedford (ANDA 76-582) currently have approved ANDAs for this drug product.

6. Vacant RLD = Corlopam Injection (10mg/base)/mL 1mL amp.
 Deputy Dir. DLPS 2mL amp.
 Date _____
 Initials _____
 7. Peter Rickman Abbott Laboratories, Hospital NDA 9-922 (001)
 Director, DLPS Hospira Inc. Products Division Date 2/15/05
 Initials _____

Para. IV Patent Cert: Yes No ; Pending Legal Action: Yes No ; Petition: Yes No
 Comments: Bioequivalence review - bio waiver granted under 21 CFR 320.22 (b)(1). Drug product is "Q+Q" to the RLD. Office level prepared 11/15/04. Microbiology/sterility assurance found acceptable 2/9/05. FPL found acceptable for approval 1/26/05. I-422 exclusivity has been addressed under BPCA. CMC found acceptable for approval 2/10/05. Methods validation was not requested - both the API and drug products are compendial.

8. Robert L. West Date 2/15/2005
 Deputy Director, OGD Initials Robert West
 Para. IV Patent Cert: Yes No ; Pending Legal Action: Yes No ; Petition: Yes No
 Comments: Acceptable EES dated 1/21/05 (verified 2/15/05) No. A.F. Alerts noted. There are no unexpired patents currently listed in the "Orange Book" for this drug product.

This ANDA is recommended for approval.

9. Gary Buehler Date _____
 Director, OGD Initials _____
 Comments:
 First Generic Approval PD or Clinical for BE Special Scientific or Reg. Issue

10. Project Manager, Team Simon Eng Date 2/15/05
 Review Support Branch Initials _____
 N/A Date PETS checked for first generic drug (just prior to notification to firm)
 Applicant notification:
10 AM Time notified of approval by phone 10:46 AM Time approval letter faxed
 FDA Notification:
2/15/05 Date e-mail message sent to "CDER-OGDAPPROVALS" distribution list.
2/15/05 Date Approval letter copied to \\CDS014\DRUGAPP\ directory.

OCT 25 2004

36. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: #77-155

APPLICANT: Sabex 2002, Inc.

DRUG PRODUCT: Fenoldopam Mesylate Injection USP, 10mg/1mLl and 20mg/2mL

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. The DMF # (b) (4) was reviewed and found to be inadequate. Please do not respond until the DMF holder has responded to their deficiencies.

2.

3.

4.

5.

6.

7.

(b) (4)

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. Please provide current room temperature stability data.
2. The labeling information that you have provided is under review . The deficiencies found will be communicated to you under a separate cover.
3. The bioequivalence information that you have provided is currently under review. After this review is completed, any deficiencies found will be communicated to you under a separate cover.

4. The information submitted on sterility is currently under review by our Microbiology team. Any deficiencies found will be communicated to you under a separate cover.

Sincerely yours,

A handwritten signature in cursive script, appearing to read "Rashmikant Patel".

Rashmikant Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 77-155 Final Check List for Branch Chief

- 1) Check letter date and stamp date of ANDA vs. drafted letter.
- 2) Check for any NC arriving post stamp date but prior to Reg. Review.
- 3) Check for gross errors in letter.
- 4) Check that correct letter format is used. (PIV vs. Other acknowledgment)
- 5) Check address and contact person on letter vs. 356h.
- 6) Check for any t-cons and verify date and correspondence date.
- 7) Check Patent Certification information in entered in COMIS (by Eda) vs. Actual certification. If multiple patent certifications, should be based on PIV if applicable or latest expiring patent.
- 8) Check for any comments or problems raised by reviewer on Check List.
- N/A 9) If first generic, copy BE review and file.
- 10) Sign Check List.
- 11) Check electronic Orange Book to verify current patent information and correct RLD. Corlopam
- N/A 12) Check for MOU patents
- 13) Review 356h. Check NDA number and RLD for correct reference. If proprietary name proposed, notify Labeling reviewer.
- 14) Review Basis for Submission. Corlopam 19-922
- 15) Review Patent Certifications and Exclusivity Statement. (If an expiration of an exclusivity has occurred make a note to the Labeling reviewer.
- 16) Review Comparison between Generic Drug and RLD for: condition of use, active ingredients, route of administration, dosage form and strength. Check Components and Composition.
- 17) Sign cover letter 505 (j)(2)(A) OK, date, and full signature.
- 18) Pull USP information. (USP ___ yes ___ no)
- 19) Final Grammar review on letter.
- 20) Verify information in OGD Patent Tracking System.
- 21) EES slip.
- 22) Document in record book.

Signature _____ date _____

ANDA CHECKLIST
FOR COMPLETENESS and ACCEPTABILITY of an APPLICATION

ANDA Nbr: 77-155 FIRM NAME: SABEX 2002

RELATED APPLICATION(S): NA

First Generic Product Received? NO

DRUG NAME: FENOLDOPAM MESYLATE

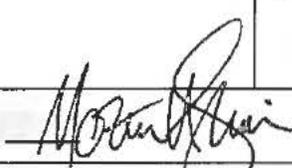
DOSAGE FORM: INJECTION USP, 10 MG/ML

Bio Assignments:	<input checked="" type="checkbox"/> Micro Review
<input checked="" type="checkbox"/> BPH	
<input type="checkbox"/> BCE	
<input type="checkbox"/> BST	

Random Queue: 1

Chem Team Leader: Mueller, Albert PM: Simon Eng Labeling Reviewer: James Barlow

Letter Date: MAY 20, 2004	Received Date: MAY 24, 2004
Comments: EC-1 YES	On Cards: YES
Therapeutic Code: 1020100 ANTI - HYPERTENSIVE AGENTS	
Archival Format: PAPER	Sections I (356H Sections per EDR Email)
Review copy: YES	E-Media Disposition: NO
Not applicable to electronic sections	
Field Copy Certification (Original Signature) YES	
Methods Validation Package (3 copies PAPER archive) (Required for Non-USP drugs) YES	
Cover Letter YES	Table of Contents YES
PART 3 Combination Product Category N Not a Part3 Combo Product (Must be completed for ALL Original Applications) Refer to the Part 3 Combination Algorithm	

Reviewing CSO/CST Christine Bina Date 7/9/04	Recommendation: <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE to RECEIVE
Supervisory Concurrence/Date: 	Date: 21 July 2004
ADDITIONAL COMMENTS REGARDING THE ANDA: 1) Need to change RLD holder to Hospira on 356h and Basis for Submission 2) Need to address the I-422 exclusivity 3) Need differences annotated and explained for side by side labeling 4) Need Reprocessing Statement 5) Ask for Engenering drawings of container 6) Need sample statement	
Top 200 Drug Product:	

APPEARS THIS WAY ON
ORIGINAL

Sec. I	Signed and Completed Application Form (356h) YES (Statement regarding Rx/OTC Status) RX YES Need to change RLD holder to Hospira	☒
Sec. II	Basis for Submission NDA# : 19-922 Ref Listed Drug: CORLOPAM Firm: ABBOTT LABORATORIES ANDA suitability petition required? NO If Yes, then is change subject to PREA (change in dosage form, route, active ingredient) For products subject to PREA a wavier request must be granted prior to approval of ANDA. <div style="text-align: right;">Wavier Granted:</div>	☒
Sec. III	Patent Certification 1. Paragraph: I 2. Expiration of Patent: NA None A. Pediatric Exclusivity Submitted? B. Pediatric Exclusivity Tracking System checked? Exclusivity Statement: YES Need to address the I-422 exclusivity-Will now carve out	☒
Sec. IV	Comparison between Generic Drug and RLD-505(j)(2)(A) 1. Conditions of use Y 2. Active ingredients Y 3. Route of administration Y 4. Dosage Form Y 5. Strength Y	☒
Sec. V	Labeling (Mult Copies N/A for E-Submissions) 1. 4 copies of draft (each strength and container) or 12 copies of FPL Y- 1mL and 2 mL amps 2. 1 RLD label and 1 RLD container label Y 3. 1 side by side labeling comparison with all differences annotated and explained Need differences annotated and explained 4. Was a proprietary name request submitted? No (If yes, send email to Labeling Rvwr indicating such.)	☒
Sec. VI	Bioavailability/Bioequivalence 1. Financial Certification (Form FDA 3454) and Disclosure Statement (Form 3455) NO 2. Request for Waiver of In-Vivo Study(ies): YES 3. Formulation data same? (Comparison of all Strengths) (Ophthalmics, Otics, Topicals Perenterals) Q1 & Q2 4. Lot Numbers of Products used in BE Study(ies): 5. Study Type: IN-VIVO PK STUDY(IES) (Continue with the appropriate study type box below)	☒
Study Type	IN-VIVO PK STUDY(IES) (i.e., fasting/fed/sprinkle) NA a. Study(ies) meets BE criteria (90% CI or 80-125, Cmax, AUC) b. EDR Email: Data Files Submitted: NO c. In-Vitro Dissolution: NO	☐

Study Type	IN-VIVO BE STUDY with CLINICAL ENDPOINTS NO a. Properly defined BE endpoints (eval. by Clinical Team) b. Summary results meet BE criteria (90% CI within +/- 20% or 80-120) c. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo (p<0.05) (eval. by Clinical Team) d. EDR Email: Data Files Submitted	<input type="checkbox"/>
Study Type	TRANSDERMAL DELIVERY SYSTEMS NO a. <u>In-Vivo PK Study</u> 1. Study(ies) meet BE Criteria (90% CI or 80-125, Cmax, AUC) 2. In-Vitro Dissolution 3. EDR Email: Data Files Submitted b. <u>Adhesion Study</u> c. <u>Skin Irritation/Sensitization Study</u>	<input type="checkbox"/>
Study Type	NASALLY ADMINISTERED DRUG PRODUCTS NO a. <u>Solutions</u> (Q1/Q2 sameness): 1. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming, Tail Off Profile) b. <u>Suspensions</u> (Q1/Q2 sameness): 1. In-Vivo PK Study a. Study(ies) meets BE Criteria (90% CI or 80-125, Cmax, AUC) b. EDR Email: Data Files Submitted 2. In-Vivo BE Study with Clinical EndPoints a. Properly defined BE endpoints (eval. by Clinical Team) b. Summary results meet BE criteria (90% CI within +/- 20% or 80-120) c. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo (p<0.05) (eval. by Clinical Team) d. EDR Email: Data Files Submitted 3. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming, Tail Off Profile)	<input type="checkbox"/>
Study Type	TOPICAL CORTICOSTEROIDS (VASOCONSTRICTOR STUDIES) NO a. Pilot Study (determination of ED50) b. Pivotal Study (study meets BE criteria 90%CI or 80-125)	<input type="checkbox"/>
Sec. VII	Components and Composition Statements 1. Unit composition and batch formulation Y 2. Inactive ingredients as appropriate Y-Q1 & Q2	<input checked="" type="checkbox"/>

<p>Sec. VIII</p>	<p>Raw Materials Controls</p> <p>1. Active Ingredients</p> <p>a. Addresses of bulk manufacturers Y</p> <p>b. Type II DMF authorization letters or synthesis Y-DMF# (b) (4)</p> <p>c. COA(s) specifications and test results from drug substance mfgr(s) Vol. 3</p> <p>d. Applicant certificate of analysis vol. 3</p> <p>e. Testing specifications and data from drug product manufacturer(s) Y</p> <p>f. Spectra and chromatograms for reference standards and test samples Y</p> <p>g. CFN numbers</p> <p>2. Inactive Ingredients</p> <p>a. Source of inactive ingredients identified Y-vol. 4</p> <p>b. Testing specifications (including identification and characterization) Y</p> <p>c. Suppliers' COA (specifications and test results) Y</p> <p>d. Applicant certificate of analysis</p>	<p>☒</p>
<p>Sec. IX</p>	<p>Description of Manufacturing Facility</p> <p>1. Full Address(es) of the Facility(ies) vol. 1</p> <p>2. CGMP Certification: YES</p> <p>3. CFN numbers 9615155</p>	<p>☒</p>
<p>Sec. X</p>	<p>Outside Firms Including Contract Testing Laboratories</p> <p>1. Full Address Y- vol. 1</p> <p>2. Functions</p> <p>3. CGMP Certification/GLP</p> <p>4. CFN numbers</p>	<p>☒</p>
<p>Sec. XI</p>	<p>Manufacturing and Processing Instructions</p> <p>1. Description of the Manufacturing Process (including Microbiological Validation, if Appropriate) Y</p> <p>2. Master Production Batch Record(s) for largest intended production runs (no more than 10x pilot batch)</p> <p>(b) (4)</p> <p>3. If sterile product: (b) (4)</p> <p>4. Filter validation (if aseptic fill) NA</p> <p>5. Reprocessing Statement NEED</p>	<p>☒</p>
<p>Sec. XII</p>	<p>In-Process Controls</p> <p>1. Copy of Executed Batch Record with Equipment Specified, including Packaging Records (Packaging and Labeling Procedures), Batch Reconciliation and Label Reconciliation Lot# 1760311</p> <p>(b) (4)</p>	<p>☒</p>
<p>Sec. XIII</p>	<p>Container</p> <p>1. Summary of Container/Closure System (if new resin, provide data) Y</p> <p>2. Components Specification and Test Data (Type III DMF References) Y-DMF# (b) (4)</p> <p>letter in vol. 1</p> <p>3. Packaging Configuration and Sizes Y</p> <p>4. Container/Closure Testing NA</p> <p>5. Source of supply and suppliers address Y</p>	<p>☒</p>

Sec. XIV	Controls for the Finished Dosage Form 1. Testing Specifications and Data Y 2. Certificate of Analysis for Finished Dosage Form Y-vol. 3- lot#1760311	<input checked="" type="checkbox"/>
Sec. XV	Stability of Finished Dosage Form 1. Protocol submitted Y 2. Post Approval Commitments Y-vol-5 3. Expiration Dating Period (b) (4) 4. Stability Data Submitted a. 3 month accelerated stability data Y-lot#170311A b. Batch numbers on stability records the same as the test batch	<input checked="" type="checkbox"/>
Sec. XVI	Samples - Statement of Availability and Identification of: 1. Drug Substance 2. Finished Dosage Form 3. Same lot numbers	<input checked="" type="checkbox"/>
Sec. XVII	Environmental Impact Analysis Statement Y-p.vol. 1	<input checked="" type="checkbox"/>
Sec. XVIII	GDEA (Generic Drug Enforcement Act)/Other: 1. Letter of Authorization (U.S. Agent [if needed, countersignature on 356h]) US Agent letter -vol. 1 2. Debarment Certification (original signature): YES 3. List of Convictions statement (original signature) Y	<input checked="" type="checkbox"/>

ANDA 77-155

Roundtable Healthcare Partners
U.S. Agent for: SABEX 2002 INC
Attention: George S. Zorich
272 E. Deerpath St., Suite 350
Lake Forest, IL 60045

JUL 21 2004

Dear Sir:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is made to the telephone conversation dated July 14, 2004 and your correspondence dated July 19, 2004.

NAME OF DRUG: Fenoldopam Mesylate Injection USP, 10 mg/mL,
1 mL and 2 mL ampoules

DATE OF APPLICATION: May 20, 2004

DATE (RECEIVED) ACCEPTABLE FOR FILING: May 24, 2004

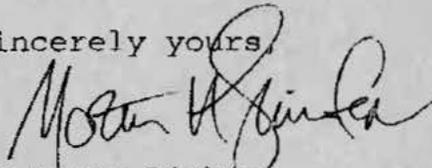
We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Simon Eng
Project Manager
(301) 827-5848

Sincerely yours,



Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 77-155

cc: DUP/Jackets

HFD-600/Division File

Field Copy

HFD-610

HFD-92

Endorsement:

HFD-615/MShimer, Chief, RSB *[Signature]* date 21 Jul 04

HFD-615/CBina, CSO *[Signature]* date 7/21/04

Word File V:\Firmsn2\Sabex\ltrs&rev\77155.ACK

F/T

ANDA Acknowledgment Letter!