CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40347

BIOEQUIVALENCY REVIEW(S)

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 40-347 APPLICANT: Bedford Laboratories™

DRUG PRODUCT: Leucovorin Calcium Injection
10 mg (base)/1 mL; 30 mL/vial & 50 mL/vial

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

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

Sincerely yours,

/S/

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

Leucovorin Calcium Injection
10 mg (base)/1 mL; 30 mL/vial & 50 mL/vial
ANDA # 40-347
Reviewer: Sikta Pradhan
WORD:X:\Pradhan\40347W.N98

Bedford Laboratories™
Bedford, OH
Submission Date:
November 19, 1998
December 16, 1998

Review of a request for Waiver of In-Vivo Bioequivalenc Study

The firm has submitted this application (dated November 19, 1998) to the Agency requesting a waiver of in vivo bioequivalence study requirements for its Leucovorin Calcium Injection, USP, 10 mg(base)/mL; 30 mL/vial (single dose) and 50 mL/vial.(single dose). The firm has stated in this submission that its proposed test product contain the same active and inactive ingredients as does the reference listed drug (RLD), Abbott's Leucovorin Calcium Injection, 10 mg/mL;10 mL and 25 mL per vial.

On December 16, 1998, the firm has submitted an amendment to this application informing the Agency that the RLD for this application has been changed to Immunex's Leucovorin Calcium Injection , 350 mg base, lyophilized powder, single dose vial, final concentration of 20 mg/mL when reconstituted.

The Bedford's application for the 30 mL/vial and 50 mL/vial is based on the approval of Gensia Laboratories' petitions pursuant to 21 U.S.C. 505(j)(2)(c) and CFR 314.93 that requested a change from the listed drug described in the above paragraph. The ANDA Suitability Petitions were submitted under, Docket Nos., 97P-0502/CP2 for 30 mL/vial, and 97P-0502/CP1 for 50 mL/vial. The petitions were approved on March 31, 1998. In these Petitions, the RLD used is Immunex's Leucovorin Calcium Injection , 350 mg/vial (concentration, 20 mg/mL).

Formulation Comparison:

Excipient	Ref. Listed Drug (Immunex's 350 mg/vial)	Proposed Drug (Bedford's 30 mL/vial)	Proposed Drug (Bedford's 50 mL/vial
Leucovorin Ca^{+2}		10 mg (base)/mL	10 mg (base)/mL
Drug Content	350 mg (base)/vial	300 mg (base)/vial	500 mg (base)/vial
Sodium Chloride	8 mg/mL	8 mg/mL	8 mg/mL
Sodium Hydroxide	For pH adjustment	For pH adjustment	For pH adjustment
Hydrochloric Acid	For pH adjustment	For pH adjustment	For pH adjustment
Water for Injection,USP	qs	qs	qs
Dosage form	Lyophilized powder for single administration	Liquid for single Administration	Liquid for single administration

Comments:

1. The drug is classified as "AP" in the list of the "approved Drug Products with Therapeutic Equivalence".
2. The conditions of use for the proposed drug product and the listed drug are identical.
3. The inactive ingredients used in the proposed drug products are identical in type and quantity as in the listed drug.
4. Both the test and reference products are labeled for Intravenous or Intramuscular administration.
5. The waiver is granted.

Recommendation:

The Division of Bioequivalence agrees that the information submitted by Bedford Laboratories demonstrates that its Leucovorin Calcium Injection, 10 mg/mL; 30 mL Vials and 50 mL Vials falls under 21 CFR Section 320.24 (b)(6) of the Bioavailable/Biequivalence Regulations. The waiver of in vivo bioequivalence study for the proposed test product is granted. From the bioequivalence point of view, the application is acceptable.

/S/

Sikta Pradhan, Ph. D.
Division of Bioeqivalence
Review Branch I

RD INITIALED YCHUANG /S/ 1/22/99
FT INITIALED YCHUANG

Concur: /S/ 1/25/99
Dale P. Conner, Pharm.D.
Director, Division of Bioequivalence

cc: ANDA # 40-347W.N98 (original, duplicate), HFD-652 (Huang, Pradhan), HFD-650 (Director), Drug File, Division File.

OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE

ANDA# 40-347 SPONSOR :Bedford Laboratories
DRUG & DOSAGE FORM : Leucovorin Calcium Injection
STRENGTH (s) : 10 mg/mL; 30 mL/vial and 50 mL/vial
TYPE OF STUDY: Waiver of Bioequivalence Study
STUDY SITE: N/A

STUDY: See Review

Waiver----Acceptable.

DISSOLUTION CONDITIONS: N/A

PRIMARY REVIEWER : Sikta Pradhan
BRANCH : I
INITIAL : _____ DATE : 1/22/99

BRANCH CHIEF : Yih Chain Huang
BRANCH : I
INITIAL : _____ DATE : 1/22/99

DIRECTOR : Dale P. Conner
DIVISION OF BIOEQUIVALENCE

INITIAL : _____ DATE : 1/25/99

DIRECTOR : Douglas L. Sporn
OFFICE OF GENERIC DRUGS

INITIAL : _____ DATE : _____