CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

50-809

CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW(S)

NDA#	50-809
PRODUCT	Azithromycin
FORMULATION	Sterile Powder for injection
DOSAGE STRENGTHS	500 mg/vial and 2.5 g/vial
SUBMISSION DATE	August 2, 2005
SUBMISSION TYPE	New Drug Application 505(b)(2)
SPONSOR	SICOR Pharmaceuticals, Inc.; 19 Hughes, Irvine, CA 92618
OCPB DIVISION	Division of Clinical Pharmacology IV
MEDICAL DIVISION	Division of Antiinfective and Opthalmalogic Drug Products
REVIEWER	Jeffrey J. Tworzyanski, Pharm.D.
TEAM LEADER	Venkat R. Jarugula, Ph.D.

CLINICAL PHARMACOLOGY & BIOPHARMACEUTICS REVIEW

1 EXECUTIVE SUMMARY

SICOR Pharmaceuticals submitted a 505(b)(2) New Drug Application for Azithromycin for Injection on August 2, 2005. Azithromycin is a broad-spectrum semi-synthetic macrolide antibiotic chemically related to erythromycin and clarithromycin. Azithromycin for injection is indicated for the treatment of patients with infections caused by susceptible strains of the microorganisms in the conditions listed below:

- Community-acquired pneumonia due to *Chlamydia pneumoniae*, *Haemophilus influenzae*, *Legionella pneumophila*, *Moraxella catarrhalis*, *Mycoplasma pneumoniae*, *Staphylococcus aureus*, or *Streptococcus pneumoniae* in patients who require initial intravenous therapy.
- Pelvic inflammatory disease due to *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, or *Mycoplasma hominis* in patients who require intravenous therapy.

SICOR relies upon the safety and effectiveness of Pfizer's Zithromax® (Azithromycin for Injection) as the previously approved drug under NDA 50-733, in seeking approval of their proposed product Azithromycin for Injection, 500 mg/vial and 2.5g/vial. Zithromax is formulated using azithromycin dehydrate. SICOR's Azithromycin for Injection is formulated using the same active pharmaceutical moiety (but a different salt form, azithromycin hydrogen citrate) and inactive ingredients, and offered in the same dosage form, strength, and route of administration as Pfizer's Zithromax®. Additionally, SICOR is proposing a pharmacy bulk single-use vial, offered at 2.5 g vial to be reconstituted to 100mg/ml, the same concentration as Pfizer's Zithromax®. SICOR's proposed drug products are manufactured using a different form of azithromycin, azithromycin hydrogencitrate rather than azithromycin dihydrate. Once reconstituted as directed in the package insert, SICOR's drug product contains the same active pharmaceutical moiety and inactive ingredients in the same concentrations as Pfizer's Zithromax®. Therefore, SICOR Pharmaceuticals, Inc.'s request for a waiver of performing a bioavailability/bioequivalence study in accordance with 21CFR §320.22(b) (1) is acceptable.

1.1 RECOMMENDATIONS

The Office of Clinical Pharmacology, Division of Clinical Pharmacology IV (OCP/DCP IV) has reviewed NDA 50809. The submission is acceptable from a Clinical Pharmacology point of view. The sponsor's request for a waiver of performing an in vivo bioavailability/bioequivalence study is acceptable.

1.2 PHASE IV COMMITMENTS

There are no phase IV commitments.

1.3 SUMMARY OF CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS FINDINGS

The reference listed drug is Pfizer's Zithromax® for injection which is formulated using azithromycin dihydrate. SICOR's Azithromycin for Injection is formulated using azithromycin hydrogencitrate. Table 1 shows a comparison of the formulation of Pfizer's Zithromax® for injection versus SICOR's Azithromycin. Table 2 shows a comparison of reconstituted Zithromax® for Injection.

Table 1 Comparison of Vial Contents: SICOR's Azithromycin for injection with Pfizer's Zithromax® (azithromycin for injection)

Ingredient	Function	Pfizer's Zithromax®	SICOR's Azithromycin for Injection	
		500mg/vial	500mg/vial	2.5 g/vial
Azithromycin (free base)	Active Drug	500mg/vial [1]	500 mg/vial [2]	2.5 g/vial [2]
Citric Acid	—	413.6 mg/vial [3]	—	—
Sodium Hydroxide	—	—	—	—

[1] Listed in package insert for Zithromax® as containing Azithromycin Dihydrate equivalent to 500 mg of Azithromycin.

[2] Manufactured using Azithromycin Hydrogencitrate equivalent to 500mg and 2.5g of Azithromycin, respectively.

[3] Listed in package insert for Zithromax® under **HOW SUPPLIED**

Table 2 Comparison of Reconstituted Solutions: SICOR's Azithromycin for Injection with Pfizer's Zithromax® (azithromycin for injection)

Ingredient	Pfizer's Zithromax®	SICOR's Azithromycin for Injection
	500mg/vial	500mg/vial or 2.5g/vial
Azithromycin (free base)	100mg/ml	100mg/ml
Citric Acid	[redacted]	[redacted]
pH	[redacted]	[redacted]
Sodium Hydroxide	[redacted]	[redacted]

[redacted]. Since the proposed product is for intravenous use only and contains the same active moiety and inactive ingredients as the Reference Listed Drug, Zithromax, the FDA is willing to accept a comparison of the composition of the two products in lieu of an in vivo bioavailability/bioequivalence study and waive the requirement of performing an in vivo bioavailability/bioequivalence study as per 21 CFR 320.22(b)(1)(i).

Jeffrey J.Tworzyanski, Pharm.D.
Office of Clinical Pharmacology
Division of Clinical Pharmacology IV

RD/FT Initialed by Venkat R. Jarugula, Ph.D.
Team Leader

cc:
Division File: NDA 50-809
HFD-520 (CSO/DeBellas)
HFD-520 (MO/Moledina)
HFD-520 (Chemistry/Yu)
HFD-880 (Division File, Lazor, Selen, Jarugula, Tworzyanski)
CDR (Clin. Pharm.)

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/s/

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BIOPHARMACEUTICS

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5/26/2006 02:51:51 PM
BIOPHARMACEUTICS