CLINICAL PHARMACOLOGY REVIEW

NDA: 50-795	Submission Date: 10/8/12
Drug	Doxycycline Hyclate
Trade Name	DORYX™
OCP Reviewer	Ryan P. Owen, Ph.D.
OCP Team Leader	Kimberly L. Bergman, Pharm.D.
OCP Division	DCP4
OND division	DAIP
Sponsor	Warner Chilcott
Relevant IND(s)	IND (b) (4)
Submission Type; Code	Efficacy Supplement; SE2-010 Resubmission
Formulation; Strength(s)	200 mg delayed-release tablet
Indication	Treatment of uncomplicated urethral, endocervical, or rectal infection in adults caused by *Chlamydia trachomatis*: 100 mg by mouth twice a day for 7 days or 200 mg by mouth once a day for 7 days.

1. EXECUTIVE SUMMARY

The Sponsor currently markets DORYX (WC2031, doxycycline hyclate) tablets in 75 mg, 100 mg, and 150 mg. On 5/28/09 the Sponsor submitted a prior approval supplement (S-0010, SDN068) to add a 200 mg dosage form. Two clinical pharmacology studies were included in this submission, a bioequivalence study (two 100 mg tablets compared to one 200 mg tablet) and a food effect study. Although the clinical pharmacology studies were acceptable, this submission received a complete response letter on 9/29/09 because there was no approved indication which required a 200 mg tablet and having an unnecessary dosage strength on the market could lead to medication errors.

The Sponsor proposed an indication of uncomplicated urogenital *Chlamydia trachomatis* for the 200 mg dosage form. The Division indicated that the Sponsor's proposed indication would be acceptable, but it would require a Phase 3 non-inferiority trial. On 11/22/10, the Sponsor resubmitted the NDA for the 200 mg dosage form. In addition to the Phase 3 trial, the Sponsor also submitted another clinical pharmacology study (multiple dose doxycycline bioavailability). Refer to the clinical pharmacology review in DARRTS (dated 4/26/11 under NDA 50-795) for all relevant study reports. Due to the presence of clinical data, the original chemistry supplement was recoded as an efficacy supplement (SE2-010). On 7/1/11, the resubmission received a complete response letter due to statistical issues.

Subsequently, the Sponsor entered a dispute resolution procedure, and resubmitted the NDA for a third time on 10/8/12 (the current submission). There were no new clinical studies in the current submission; therefore, the scope of this review is limited to labeling recommendations based on the previously conducted clinical pharmacology studies.

1.1 Recommendation

The Office of Clinical Pharmacology, Division 4 has reviewed SE2-010 for NDA 50-795, and it is acceptable from a clinical pharmacology perspective. The labeling recommendations included in this review should be forwarded to the Sponsor.

1.2 Phase 4 Commitments

None.

1.3 Summary of Important Clinical Pharmacology and Biopharmaceutics Findings (from previous reviews)

- One WC2031 200 mg tablet was found to be bioequivalent to two WC2031 100 mg tablets.
- The pharmacokinetics of doxycycline are not altered when one WC2031 200 mg tablet is administered to healthy subjects in a fed state versus a fasted state.
- The multiple dose pharmacokinetic parameters of WC2031 were determined following seven days of once daily administration. Steady-state was reached by Day 5.

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Ryan P. Owen, Ph.D.

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Kimberly L. Bergman, Pharm.D.

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Reviewer's Recommendation

The Sponsor's proposed changes are acceptable and should be included in the revised label.

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/s/

RYAN P OWEN
01/18/2013

KIMBERLY L BERGMAN
01/18/2013