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.

Ryan P. Owen, Ph.D.

Kimberly L. Bergman, Pharm.D.
Reviewer’s Recommendation

The Sponsor’s proposed changes are acceptable and should be included in the revised label.
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

RYAN P OWEN
01/18/2013

KIMBERLY L BERGMAN
01/18/2013