Pharmacokinetic Assessment of Rate-Controlling Mechanism of Remoxy, an Extended-Release Oxycodone Formulation

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Abstract

Introduction: Remoxy® is an extended-release oxycodone formulation designed to provide therapeutic benefits of fentanyl and morphine by controlling the rate of drug delivery. The objective of this study was to assess the rate-controlling mechanism of Remoxy, an extended-release oxycodone formulation.

Methods: Two phase I, single-center, randomized, open-label, active-controlled, 3-way crossover PK studies were conducted in healthy volunteers (aged 18–45) to evaluate oxycodone absorption after oral administration of Remoxy 40 mg capsule, fed, and an oral dose of immediate-release (IR) oxycodone 20 mg capsule, fasted.

Results: Buccal dissolution of 40 mg Remoxy® (fed) resulted in lower Cmax and lower early partial AUCs compared with the oral dose of oxycodone IR 20 mg capsule, fasted. These results suggest that Remoxy® does not result in dose dumping, as evidenced by the lack of immediate sharp peaks in plasma concentration-time profiles indicating that no dose dumping occurs.

Study Design

Study A: Buccal Dissolution of 40 mg Remoxy® (fed)

Inclusion criteria were similar in both studies. Eligible subjects were men and non-pregnant women aged 18–45, in good health, free of any drug or medical therapy, and had body mass index (BMI) between 19–29. Subjects were not permitted to use other prescription drugs (except hormonal contraceptives) within 14 days or over-the-counter medications, alcohol, grapefruit, grapefruit juice, caffeine, or xanthine-containing medications within 30 days of the study.

Blood samples were collected at baseline and 2 hours post-dose. Plasma samples were assayed using a liquid chromatography–mass spectrometry method. The method was linear over the range of 2–1000 ng/mL. Inter-assay precision and accuracy were determined using 6 points on the calibration curve.

Safety assessments included a physical examination, measurement of vital signs, evaluation of electrocardiograms and clinical laboratory tests, and review of adverse events and serious adverse events.

Statistical Analysis

All analyses were performed at a 2:1 ratio of study drug included in the safety analysis. 48 subjects were enrolled in the study and 46 were evaluable (2 per treatment sequence). The sample size was determined to provide 90% power to detect a difference in Tmax of 10% or greater. Comparisons were made using an analysis of variance model with factors for sequence, subject within sequence, period, and treatment.

Conclusions: Buccal dissolution of Remoxy® resulted in a significant delay in Tmax, lower Cmax, and lower early partial AUCs relative to the oral dose of oxycodone IR 20 mg capsule, fasted. These results suggest that Remoxy® does not result in dose dumping, as evidenced by the lack of immediate sharp peaks in plasma concentration-time profiles indicating that no dose dumping occurs.

References