A Comparative Pharmacokinetic Study of Omeprazole in a Fixed-Dose Combination Capsule of Meloxicam/Omeprazole Compared to the Individual Omeprazole Capsule in Healthy Adult Volunteers under Fed Conditions

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Purpose
Clinical trials supporting development of fixed-dose combination (FDC) products (in which the individual components/drugs have been previously approved) are usually submitted in the EU using Article 10b of 2001/83/EC and in the US by the 505(b)(2) NDA route. As part of such program, one of the objectives of this study was to provide bioequivalence data for the omeprazole component of a meloxicam/omeprazole fixed-dose combination capsule to a commercially available comparator omeprazole capsule formulation (Losec®).

Methods
Healthy male and female subjects were randomized in a crossover study design. After a supervised overnight fast, subjects received a high-fat (approximately 50% of total caloric content of the meal), high-calorie (approximately 800 to 1000 kcal) meal 30 minutes before dosing. They received a single oral dose of meloxicam/omeprazole FDC 15 mg/20 mg capsule (T) and omeprazole 20 mg capsule (Losec®) (R). A washout period of 14 days separated treatment sequences. Blood samples were collected over a period of 14 hours for omeprazole. Safety evaluations included AEs monitoring, laboratory tests, vital signs and ECG. Plasma concentrations were assayed for omeprazole with a validated HPLC method using MS/MS detection. PK parameters were calculated using a NCA approach. The primary pharmacokinetic parameters were AUC and Cmax.

Results
A total of 48 subjects were enrolled in the study, and 44 subjects were included in the comparison of interest. Following administration of the combination capsule with meloxicam, the omeprazole mean Cmax and AUC values were 219 ng/mL and 729 ng*h/mL, respectively; similar results were observed when omeprazole was administered alone (p > 0.05). The Cmax and AUC T/R ratio of geometric LSmeans (90% CI) was 96% (82, 113) and 102% (93, 111), respectively. Meloxicam did not affect the time to Cmax of omeprazole (median 6 hours vs 5 hours, p > 0.05). Each of the treatments was well tolerated; no SAEs were reported.

Conclusion
The omeprazole component in the meloxicam/omeprazole combination capsule was bioequivalent to that of a corresponding dose of omeprazole capsule administered alone, following single dose administration under fed conditions.