Metformin IR tablets: partial in vitro dissolution profiles differences do not preclude in vivo bioequivalence

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Abstract— Objectives: To investigate whether Metformine Profarma 850 mg tablets (test product) are bioequivalent to Glucophage® 850 mg tablets (Merck Santè laboratories - reference product) despite partial in vitro dissolution profiles differences observed.
Methods: A randomized, open-label, single-dose, two-period, one-week wash out, crossover study was performed in 20 healthy male and female volunteers at "Mother Theresa" University Hospital Centre, Tirana, Albania, after obtaining the approval by National Ethics Committee. A single 850mg dose of metformin was administrated with 200 ml of water after overnight fasting and blood samples were collected at 0, 0.5, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 8, 10, 12 and 14 h after dosing. Plasma concentrations were measured by using a validated ion-pair HPLC method with UV-DAD. Non-compartmental pharmacokinetic parameters such as Cmax, AUC0-14 h, AUC0-inf, and Tmax were determined using PKSolver Version 2.
Results: Administration of single Metformin Profarma 850 mg and Glucophage® 850 mg tablets resulted in comparable systemic exposures to metformin, as determined by Cmax, AUC0-14 and AUC0-inf. ANOVA analysis of the ln-transformed Cmax, AUC0-14 and AUC0-inf values indicated that none of the effects examined (formulation, period, sequence and carry over) was statistically significant. The geometric mean ratios of Cmax, AUC0-14 and AUC0-inf were 103.0%, 99.3% and 98.8%, respectively, and 90% confidence intervals of Cmax, AUC0-14 and AUC0-inf were contained within the bioequivalence acceptance limits of 80% to 125%.
Conclusions: Metformin Profarma 850 mg and Glucophage® 850 mg tablets were shown to be bioequivalent despite the in vitro dissolution profiles indicate a faster dissolution rate for Metformine Profarma 850 mg tablets, at least in one dissolution medium.
Keywords— metformin; dissolution profile; pharmacokinetics; bioequivalence