Bioequivalence Study of Verapamil Hydrochloride 240 mg Extended Release Tablet in Healthy Human Volunteers under Fasting Condition

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ABSTRACT

Objective: The objective of present study was to assess the bioequivalence of Verapamil Hydrochloride 240mg Extended Release Tablet [Test, Cadila Pharmaceuticals Ltd., India] versus Calan SR® Tablet containing Verapamil Hydrochloride 240mg [Reference, Abbott Gmbh and co. KG, Pfizer] in healthy human volunteers after administration of single Tablet of either test or reference formulation under fasting condition, in each period.

Methods: This single-dose, randomized, 2-period, 2- Treatment, 2- Sequence, crossover study compared the pharmacokinetic properties within healthy human male volunteers under

fasting condition. Volunteers were assigned to receive, in randomized order, a single oral dose of test formulation (A) or a reference formulation(B). Each study period was separated by a 7-days washout period. Blood samples were collected at prespecified times over a period of 48 hours after administration. An HPLC-MS/MS method was used for the estimation of plasma Verapamil and Norverapamil concentrations. A noncompartmental method was employed to determine the pharmacokinetic properties (Cmax, Tmax, AUC0–t, AUC0–_, and Thalf) to test for bioequivalence. The predetermined regulatory range of 90% CI for bioequivalence was 80% to 125%. Safety was assessed using physical examination, including vital sign measurement, and direct questioning.

Results and discussion: The study was conducted in 18 volunteers (18-45 yrs; BMI 18- 25 kg/m2). For test formulation versus the reference formulation, the least squares mean test/reference ratios of Ln(Cmax), Ln(AUC(0–t)), and Ln(AUC(0–_)) were 75.95%,100.35%,100.23%. CI for Ln(Cmax), Ln(AUC(0–t)), and Ln(AUC(0–_)) were 60.69%-95.05%, 80.31%-125.39%, 80.06%-125.48%. No Serious adverse events were found or reported by volunteers throughout the study. In this study, test formulation was not found bioequivalent to the reference formulation as per predetermined regulatory criteria.

Conclusion: These observations confirm that the test formulation of Verapamil Hydrochloride 240mg Extended release tablet was not bioequivalent with the Calan SR® but it is found to be safe