Chapter 6

Summary and Conclusion

6.0 Conclusion

The present study was undertaken to establish the bioequivalence between Levetiracetam 1000 mg extended release tablet manufactured by Ranbaxy Laboratories Limited, India and two oral doses of Keppra™ 500 mg immediate release tablet (each dose containing levetiracetam 500 mg; administered at an interval of 12 hours) of UCB Pharma, Inc., USA.

The protocol and the corresponding ICF (Informed Consent Form) used to obtain informed consent of study subjects were reviewed and approved by the Jamia Hamdard Institutional Review Board. This research was carried out in accordance with the Basic Principles defined in United States FDA 21 CFR Part 320, ICH ‘Guidance on Good Clinical Practice (2002), ICMR ‘Ethical Guidelines for Biomedical Research on Human Participants (2006)’, and the CDSCO ‘Guidance on Good Clinical Practices guidelines for Clinical Research in India’. The standard SOPs of the Clinical Pharmacology Unit (CPU) and Clinical Pharmacology and Pharmacokinetics (CPP), Ranbaxy have been adhered to in the clinical, analytical, pharmacokinetic and statistical analysis performed during the course of the present study.

The clinical phase of the study was conducted as an open label, balanced, randomized, two-treatment, two-period, two-sequence, crossover bioequivalence study in twenty four (24) healthy, adult, human, male subjects under fed condition. No adverse event was reported by the study subjects during the course of this study.

The analytical method used in the present study (i.e. Ultra Performance Liquid Chromatography Mass Spectrometric Method for the Determination of Levetiracetam in Human K3-EDTA Plasma using Didanosine as Internal Standard using Waters LC/MS/MS) was valid for the determination of Levetiracetam in human K₃ EDTA plasma over a range of 0.482 µg/mL to 36.221 µg/mL using Didanosine as an internal standard.

In the present study, 90% confidence intervals for the ratios of Test (T) and Reference (R) product averages (least-squares means) derived from the analysis of log transformed pharmacokinetic parameters AUC₀₋₄ and AUC₀₋₂₄ (96.33% and 101.58% respectively) were within the bioequivalence acceptance criteria of 80-125%, based on bioequivalence assumptions.
Based on these results, Levetiracetam 1000 mg extended release tablet manufactured by Ranbaxy Laboratories Limited was found to be bioequivalent with two oral doses of a Keppra™ 500 mg tablet (each dose containing levetiracetam 500 mg; administered 12 hourly) of UCB Pharma, Inc., in healthy, adult, male, human subjects under fed condition.

The test and reference products were well tolerated by the study subjects. The deviations reported in this study were judged unlikely to affect the bioequivalence of the products evaluated.

In conclusion, Levetiracetam extended release formulations with their favorable pharmacokinetic properties, overall safety and tolerability, and convenient once-daily dosing are expected to be an ideal add-on therapy for the treatment of partial-onset seizures and are a valuable addition to the existing treatment options available for the patients with epilepsy. The present study whose primary objective was to prove the bioequivalence of a single oral dose of Levetiracetam 1000 mg extended release tablet compared to two oral doses of Levetiracetam 500 mg tablets represents a small step towards improving patient compliance in epilepsy patients.