6.0 SUMMARY AND CONCLUSION

The present study was undertaken to launch a generic version of Olmesartan which could replace safely & successfully the innovator drug product (OLMETEC®40). Hence, the pharmacokinetic bioequivalence of two batches of olmesartan medoxomil 40 mg tablet manufacture by Ranbaxy Laboratories Limited were evaluated using OLMETEC®40 mg film coated tablet (containing 40 mg olmesartan medoxomil) manufactured by Daichii Sankyo UK Ltd, as Reference product R, following single dose oral administration in healthy, adult, male human subjects under fasting conditions.

The study protocol and the informed consent form were approved by the Fortis Hospital Institutional Review Board. The study was conducted by using an open label; balanced, randomized, cross over design in healthy, male volunteers under fasting conditions. The order of receiving the test and reference products for each subject was determined according to a SAS generated randomization schedule. The clinical study was carried out in accordance with ICH Good Clinical Practices. The standard SOP’s 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.

A high performance liquid chromatographic method, validated in terms of selectivity, linearity, sensitivity, accuracy and precision, was used for the estimation of Olmesartan in plasma. The standard curve was linear & coefficient of co-relation was found to be greater than 0.99 throughout the study.

Bioequivalence was assessed by measuring the pharmacokinetic parameters namely \( C_{\text{max}} \), \( \text{AUC}_{0-t} \) and \( \text{AUC}_{0-\infty} \) as laid down by the USFDA and DCGI guidelines.

The bioequivalence criteria used were 90% confidence intervals of ratios of LSM of log transformed data for \( C_{\text{max}} \), \( \text{AUC}_{0-t} \) and \( \text{AUC}_{0-\infty} \). The 90% confidence intervals for log transformed T/R ratios for \( C_{\text{max}} \), \( \text{AUC}_{0-t} \) and \( \text{AUC}_{0-\infty} \) were 73.09-110.90, 83.73-112.62, and 85.94-112.47 for the test product A and 78.75-119.49, 86.89-116.87 and 88.42-115.71 for the test product B respectively, thus AUC values were lying within the range. However, 90% confidence intervals for \( C_{\text{max}} \) were out of the specified range of 80-125%, which could be due to small sample size, high intrasubject variability (28.6) or formulation difference. None of the test formulation achieved bioequivalence criteria.
Hence, it is recommended that the study should be repeated with large sample size or test formulations need to be reformulated to fulfill the stated regulatory bioequivalence range of 80-125% (FDA, DCGI). The formulations were safe and well tolerated by study subjects.