Montelukast Bioequivalence Study: Quantification by Liquid Chromatography Coupled to Tandem Mass Spectrometry

E Ezzeldin1,2, M Tammam1, N AboTaleb1. 1Drug Bioavailability Center, National Organization for Drug Control and Research, Cairo, Egypt, 2College of Pharmacy, King Saud University, Riyadh, Saudi Arabia

Abstract

Bioequivalence of generic product of montelukast (Brand A) was studied in comparison with reference product Singulair® tablets. Developed rapid, sensitive and specific method to quantify montelukast and gliclazide (internal standard) in plasma using liquid chromatography coupled with electrospray tandem mass spectrometry was applied.

An open, randomized, two-period crossover study with a one-week washout interval was conducted in 24 fasting healthy volunteers. Plasma samples were obtained up to 24 hours after drug administration. The extraction of montelukast from plasma involved protein precipitation using acetonitrile. The mobile phase consists of acetonitrile: 0.1% formic acid (84:16).

ANOVA test was performed to determine the effect of model factors on the PK parameters. The two one-sided t-tests were performed on the log-transformed data to determine the 90% confidence interval (CI) for the ratio of test to reference PK parameters.

Calibration curves were linear in the concentration range of 10.00-800.00 ng/ml, and the lower limit of quantification (LLOQ) was 10.00 ng/ml. The average recovery was found to be 89.23%. Within- and between-run precision was ranged between 3.48 and 14.74 % and between 9.37% and 14.96%, respectively. Accuracy between runs was ranged between 89.45 – 101.75%.

The pharmacokinetic parameters for bioequivalence showed a normal distribution, and the variance of AUC (0-24 h), AUC (0-infinity), The geometric mean for the test /Reference (individual percent ratio was 101.8% for AUC(0-24 h), 102.8% for AUC(0-infinity), 99.1% for Cmax, 108.5% for Ke, 106.1% for T1/2, and 92.9% for Tmax (arithmetic mean of individual differences).

The bioanalytical method was successfully applied to assess bioequivalence of a montelukast 10 mg tablets. The LLOQ was sensitive enough for detecting terminal phase concentrations of the drug. This study showed that the test and reference products of montelukast met the regulatory criteria for bioequivalence following a 10 mg oral dose under fasting conditions.