In Vivo Bioequivalence Study of 500 mg Deferiprone (L1) Tablets in Healthy Thai Volunteers

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Abstract

Objectives: To compare the bioequivalent parameters of 500 mg of a generic deferiprone (L1) tablets (GPO-L-ONE®) with that of a reference formulation (Ferriprox®).

Material and Method: A randomized, single dose, two treatments, two periods, two sequences crossover study was conducted in twenty-four healthy volunteers (12 males and 12 females). Each subject received a single dose of 3 tablets of 500 mg deferiprone of both formulations with a two weeks washout period. Blood samples were collected pre-dose and 15, 30, 45, 60, 90, 120, 180, 240, 300, 360 and 480 after dosing. Levels of serum deferiprone were analyzed using a validated high performance liquid chromatography (HPLC) method.

Results: Twenty-four volunteers enrolled in both period of the present study. Pharmacokinetic parameters were determined using the non-compartment model. The time for the maximum serum concentration (T_{max}; mean±SD) for reference and generic drug were 31.8±12.75 and 43.1±27.02, respectively. The maximum serum drug concentration (C_{max}; mean±SD) were 32.3±13.2 and 27.8±12.8 □g/ml for reference and generic drug, respectively. The mean ratio of C_{max} was 0.852 with the 90%confidence interval (log transformed data) was 0.772-0.934. The area under serum concentration time curve (AUC_{0-t} and AUC_{0-inf}; mean±SD) of the reference drug were 3562.5±837.1 and 3788.4±878.6 □g-min/ml, respectively and of the generic drug were 3429.3±827.0 and 3664.9±873.6 □g-min/ml, respectively. The mean ratio and the 90%confidence interval (log transformed data) of AUC_{0-t} and AUC_{0-inf} were 0.962 (0.913-1.012) and 0.966 (0.918-1.017), respectively. Both formulations were well tolerated and no adverse effects were observed.

The results demonstrate that the 90% confidence intervals of mean ratio of AUC_{0-t} and AUC_{0-inf} fell within the acceptable range (0.80-1.25) for bioequivalent eligibility. Concerning the efficacy of deferiprone which is depended on AUC rather

than C_{max}, the 90% confidence intervals of mean ratio of C_{max} was within the acceptable range of WHO criteria for bioequivalence study (0.75-1.33). Therefore both formulations of deferiprone tablets were proven bioequivalent in healthy Thai volunteers.

Figure 1 The mean serum concentration time profile with SE bar of deferiprone in 24 subjects as normal plot (a) and semi-log plot (b)