COMPARATIVE BIOAVAILABILITY STUDY OF THREE DOSAGE FORMS OF LEVOThYroxine Sodium TABLETS FOLLOWING SINGLE DOSES IN HEALTHY SUBJECTS

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OBJECTIVE

In October 2007, the U.S. Food and Drug Administration (FDA) mandated that all manufacturers of levothyroxine tablets (T 4) should conduct single and multiple-dose bioavailability studies to ensure that the new tablet formulations were comparable in terms of bioavailability to those marketed before the new mandate. The objective of this study was to determine the bioavailability of three newly reformulated levothyroxine tablet strengths using a study design adopted from the Food and Drug Administration’s (FDA’s) guidance for Industry: levothyroxine sodium tablets – Pharmacokinetic Reference Ranges for Single and Multiple Dose Studies.

METHODOLOGY

• The design was a randomized, open-label, single-dose, three-way crossover study to determine the bioavailability of three newly reformulated levothyroxine tablet strengths.
• Subjects were randomly assigned to receive the following treatments in the 3 dosing periods:
  - Treatment A = Levothyroxine sodium 600 µg (12 x 50 µg tablets)
  - Treatment B = Levothyroxine sodium 600 µg (6 x 100 µg tablets)
  - Treatment C = Levothyroxine sodium 600 µg (3 x 200 µg tablets)

RESULTS

• Thirty-six healthy volunteers (18 male and 18 female) were enrolled and 31 subjects completed all study periods.
• The concentration-time profiles of uncorrected and baseline-corrected serum T 4 and uncorrected serum T 3 for the administration of Treatments A, B, and C are presented in Figures 1 and 2, respectively.
• The GMRs of baseline-corrected serum T 4, Cmax, AUC0-24h, and AUC0-48h for the comparisons of Treatments A, B, and C were within the 80% to 125% range indicating that the tablet strengths were proportional with respect to baseline-corrected serum T 4 exposure.
• The GMRs of uncorrected serum T 4, Cmax, AUC0-24h, and AUC0-48h for the comparisons of Treatments A, B, and C were within the 80% to 125% range indicating that the tablet strengths were proportional with respect to uncorrected serum T 4 exposure.
• The GMRs of uncorrected serum T 3, Cmax, AUC0-24h, and AUC0-48h for the comparisons of Treatments A, B, and C were within the 80% to 125% range indicating that the tablet strengths were proportional with respect to uncorrected serum T 3 exposure.

CONCLUSIONS

• The statistical analyses, and the nearly superimposable mean serum concentration-time profiles of the 3 treatments, indicate that the tablet strengths were proportional.
• The 90% CIs for the PK parameters were all within the 80% to 125% range, indicating that the 3 tablet strengths were proportional with respect to T 4 exposure.
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REFERENCES