Concentration of solithromycin was measured by LC/MS/MS in plasma samples from 24 healthy adult subjects following single oral doses of 200, 400, and 600 mg solithromycin. The study was conducted in two periods: period 1, under fasted conditions; and period 2, under fed conditions (2 eggs fried in butter, 2 strips of bacon, 2 slices of toast with butter, 4 ounces of hash brown potatoes, and 12 ounces of coffee). The pharmacokinetic parameters for solithromycin in plasma are summarized in Table 1. No significant difference in solithromycin plasma concentrations was observed between the fed and fasted states, indicating that solithromycin is safe and generally well tolerated when taken with food. 

Safety and Tolerability

Solithromycin was well tolerated at the doses studied. No SAEs or deaths were reported and no subject was discontinued due to an AE. Most frequently reported AEs were gastrointestinal and occurred at similar rates in the solithromycin dosage cohorts and placebo group. Treatment-emergent AEs were reported by 4 (10%) or more of the subjects included headache, diarrhea, nasopharyngitis, vomiting, abdominal pain, and dyspepsia. No 10 of the subjects in the 600 mg cohorts had asymptomatic, reversible, transient ALT elevations (1.1-1.4X ULN); bilirubin remained within normal range.

Food Effect Study (CE01-102)

33 TEAEs were reported by 8 (31%) of the 24 subjects; 25 of 33 AEs (75%) were considered treatment related; all AEs were mild in severity. 

Pharmacokinetic Results

Multiple Dose Study (CE01-102)

The study design and objectives are outlined in Table 2. The study was conducted in two periods: period 1, under fasted conditions; and period 2, under fed conditions (2 eggs fried in butter, 2 strips of bacon, 2 slices of toast with butter, 4 ounces of hash brown potatoes, and 12 ounces of coffee). The pharmacokinetic parameters for solithromycin in plasma are summarized in Table 3. No significant difference in solithromycin plasma concentrations was observed between the fed and fasted states, indicating that solithromycin is safe and generally well tolerated when taken with food.

Conclusions

Solithromycin was well tolerated and generally well tolerated in healthy adult subjects orally administered a single 400 mg dose or 7 daily doses of 200 mg, 400 mg, or 600 mg. Solithromycin can be administered without regard to food; tolerability may be improved when taken with food. Solithromycin exhibited non-linear PK over time with accumulation after repeat dosing at 400 mg for 5 days. Solithromycin PK parameters were statistically bioequivalent for the fed and fasted states. Ratios of least-squares means for the in-transformed Cmax, AUCinf, and AUC0-24 of the fed to fasted drug exposures were 107%, 97%, and 97%, respectively, with the 90% CIs within the 80 to 120% range. No food effect on the bioavailability of solithromycin following a single 400 mg oral dose.