Characterize and Compare the Oral Pharmacokinetics of Two Atorvastatin Formulations in Healthy Chinese Male Subjects

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**Objectives:** To characterize and compare the pharmacokinetics (PK) of atorvastatin in healthy Chinese male volunteers using nonlinear mixed effects modeling (NONMEM).

**Methods:** A randomized, crossover, three-period study was conducted in fasted healthy Chinese male volunteers. Eligible participants were randomly assigned to receive a single 20 mg of the test atorvastatin formulation once and the reference formulation twice with a 7-day wash-out period between each oral administration. Blood samples were collected up to 72 hours after dosing and the plasma concentration of atorvastatin were determined with a validated ultra-performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS). Population PK modeling was performed using NONMEM. The final models were selected based on the likelihood ratio test using objective function values and graphical goodness-of-fit.

**Results:** The PK profiles of both test and reference atorvastatin in healthy human subjects were best described by a 1-compartment PK model with parallel absorption. The population mean (SE) values of the absorption rate constant KA1 and KA2 were 1.43 (0.580) hr\(^{-1}\) and 0.595 (0.0305) hr\(^{-1}\) for the test formulation, and 0.778 (0.0552) hr\(^{-1}\) and 0.585 (0.0197) hr\(^{-1}\) for the reference formulation with a lag time of 2.79 (0.0864) and 2.95 (0.0587) hr for KA2 for the test and reference formulations, respectively. The corresponding mean (SE) values for the apparent clearance (CL/F) and the apparent volume of distribution (V\(_3\)/F) were 380 (15.3) and 360 (11.0) L/h, and 639 (42.4) and 593 (26.4) L for the test and reference formulations, respectively.

**Conclusion:** The population PK models developed in this study adequately characterize the absorption, distribution, and elimination of the two atorvastatin formulations in healthy human subjects. In general, the PK parameters appear similar for the two atorvastatin formulations.