

have a slightly lower plasma exposure to atorvastatin for a given dose (Hans Lennernäs,2003).

Atorvastatin is subject to metabolism by CYP3A4 and cellular membrane transport by OATP C and P-glycoprotein, and drug-drug interactions with potent inhibitors of these systems, such as itraconazole, nelfinavir, ritonavir, cyclosporin, fibrates, erythromycin and grapefruit juice, have been demonstrated. An interaction with gemfibrozil seems to be mediated by inhibition of glucuronidation. A few case studies have reported rhabdomyolysis when the pharmacokinetics of atorvastatin have been affected by interacting drugs. Atorvastatin increases the bioavailability of digoxin, most probably by inhibition of P-glycoprotein, but does not affect the pharmacokinetics of ritonavir, nelfinavir or terfenadine (Brown et al. 1993; Pedersen et al. 1994). Atorvastatin and its metabolites are eliminated primarily in bile following hepatic and/or extra-hepatic metabolism; however, the drug does not appear to undergo enterohepatic recirculation(Ray S K, Rege N N. 2000). Mean plasma elimination half-life of atorvastatin in humans is approximately 14 hours, but the half-life of inhibitory activity for HMG-CoA reductase is 20 to 30 hours due to the contribution of active metabolites. Less than 2% of a dose of atorvastatin is recovered in urine following oral administration. (Ray S K, Rege N N. 2000).

1.5.3 Glimepiride

Studies have shown that pharmacokinetics of glimepiride does not differ between healthy subjects and patients with type 2 diabetes. Following a single oral dose of glimepiride in healthy subjects and with multiple oral doses in patients with type 2 diabetes showed peak drug concentrations 2 to 3 hours post-dose. When glimepiride was given with meals, the mean C_{max} and AUC were decreased by 8% and 9%, respectively. Furthermore, glimepiride does not accumulate in serum following multiple dosing and the clearance of glimepiride after oral administration does not change over the 1 mg to 8 mg dose range, indicating linear