

## MUSCLE TOXICITY OF STATINS

The occurrence of serious muscle toxicity with currently marketed statins is exceedingly rare.

These include advanced age and frailty, female gender, renal insufficiency, hepatic dysfunction, hypothyroidism, and concurrent use of agents that have pharmacokinetic interactions with statins, including gemfibrozil (inhibits glucuronidation of statins) and agents that inhibit CYP3A4 (inhibit metabolism of lovastatin, simvastatin, and atorvastatin), either CYP2C9 (inhibit metabolism of fluvastatin and rosuvastatin, or CYP2C19 (rosuvastatin).

Pravastatin is not subject to CYP metabolism and may therefore be less likely than other statins to have pharmacokinetic interactions with CYP inhibitors (eg, verapamil, azole antifungals)

On the other hand, pravastatin, like other statins, is a substrate for the organic anion transporter that mediates biliary excretion, and may interact with cyclosporine, which can block the biliary excretion of these agents by interfering with this mechanism.

Finally, to date there has not been a single reported (published) case of fatal rhabdomyolysis in any patient taking fluvastatin, a synthetic statin with high first-pass hepatic extraction, low systemic exposure, and no circulating active metabolites.

