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Effects of Icosapent Ethyl (Eicosapentaenoic Acid Ethyl Ester) on Pharmacokinetic Parameters of Rosiglitazone in Healthy Subjects

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Background: Icosapent ethyl (IPE; formerly AMR101) is a high-purity prescription form of eicosapentaenoic acid (EPA) ethyl ester approved in the United States as an adjunct to diet to reduce triglyceride levels in adults with severe (>=500 mg/dL) hypertriglyceridemia. Candidates for triglyceride-lowering therapy include patients with type 2 diabetes mellitus who may be receiving rosiglitazone, a thiazolidinedione antidiabetic agent and cytochrome P450 (CYP) 2C8 substrate. The purpose of this study was to assess the effects of IPE on the pharmacokinetics (PK) of rosiglitazone. **Methods:** Subjects received a single 8-mg oral dose of rosiglitazone alone and with oral IPE 4 g/day in this open-label, crossover, drug-drug interaction study. Primary and secondary PK end points included area under the concentration-versus-time curve from time zero to infinity ($AUC_{0\text{-}inf}$; primary) and maximum plasma concentration (C_{max}; secondary) for rosiglitazone with and without IPE. **Results:** Of the 30 patients enrolled, 28 completed the study. IPE 4 g/day at steady state did not significantly change the single-dose AUC0-inf or Cmax of rosiglitazone at 8 mg. Least squares geometric mean ratios (90% confidence interval) for $AUC_{0\text{-}inf}$ and C_{max} of rosiglitazone given with IPE versus rosiglitazone alone were 0.90 (87.00-93.40) and 1.01 (92.02-109.9), respectively. No serious adverse events were reported and no subject discontinued this study due to an adverse event. **Conclusions:** At steady-state concentrations, IPE did not inhibit the metabolism of rosiglitazone, a CYP2C8 substrate. Co-administration of IPE and rosiglitazone was safe and well tolerated in this PK study of healthy adult subjects.