National AIDS Treatment Advocacy Project

Preliminary results of ongoing delavirdine-protease inhibitor interaction studies---exact text of description from Pharmacia & Upjohn

PHARMACIA & UPJOHN, INC. September 5, 1996

Subject: Delavirdine - **Protease Inhibitor Drug Interactions**

Due to the interest in use of protease inhibitors in combination with other antiretroviral agents, we are giving you notification of preliminary results of ongoing delavirdine - protease inhibitor studies in order to assist you and your patients in making treatment decisions and minimizing side effects. The following information is based on studies of small numbers of normal healthy volunteers and should be regarded as preliminary. In particular, the side effect profiles are incomplete and patients and physicians should be vigilant regarding new, unusual, more frequent or more severe adverse events.

Saquinavir: In a study in which 13 healthy volunteers received saquinavir 600 mg tid with and without delavirdine 400 mg tid, coadministration of the two drugs resulted in an increase in mean steady-state trough plasma saquinavir concentrations from 15 +/- 6 ng/mL to 84 + 57 ng/mL. When seven healthy volunteers received delavirdine 400 mg tid with and without saquinavir 600 mg tid, coadministration of the two drugs resulted in a slight reduction in the mean steady-state trough plasma delavirdine concentrations from 17 +/- 5 EM to 13 + 3 EM. There was a 13% incidence of reversible elevation of hepatocellular enzymes in the first several weeks of the delavirdine and saquinavir combination (6% Grade Ill or IV). Physicians should consider following hepatic enzymes (ALT) more frequently than usual In the first weeks of administration of that combination.

Ritonavir: In a study in which 14 healthy volunteers received ritonavir 300 mg bid with and without delavirdine 400 mg bid, coadministration of the two drugs had no effect on steady-state plasma ritonavir concentrations. When nine healthy volunteers received delavirdine 400 mg bid with and without ritonavir 300 mg bid, coadministration of the two drugs resulted In a slight reduction in mean steady-state trough plasma delavirdine concentrations. The pharmacokinetic interaction of delavirdine 400 mg tid and ritonavir 600 mg bid (consult manufacturer's complete prescribing information) has not been studied. Although a pharmacokinetic interaction between delavirdine and ritonavir at their recommended doses Is theoretically possible, no evidence of an interaction was observed at doses of delavirdine 400 mg bid and ritonavir 300 mg bid. Therefore, caution is advised when these agents are used in combination therapy at recommended doses.

Indinavir: The pharmacokinetic interaction between delavirdine and indinavir was studied with 14 healthy volunteers. Administration of delavirdine 400 mg tid with a 400 mg single-dose of indinavir resulted in a mean value of the indinavir AUC which was slightly less than the value from an 800 mg single-dose of indinavir alone. The mean indinavir AUC from a 600 mg single dose of indinavir in combination with delavirdine 400 mg tid was approximately 50% greater than that observed for indinavir 800 mg alone. indinavir had no effect on plasma delavirdine concentrations. When given in

combination with delavirdine, a dose reduction of indinavir to 400 mg or 600 mg tid should be considered (consult manufacturer's complete prescribing information).

As new information Is generated, we will communicate as necessary.

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