Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States

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Pharmacokinetic Changes (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendation
• Altered dosing during pregnancy may be required for some protease inhibitors, such as lopinavir/ritonavir (see Table 5) **(AII)**

Rating of Recommendations: *A = Strong; B = Moderate; C = Optional*

Rating of Evidence: *I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Physiologic changes that occur during pregnancy can affect drug absorption, distribution, biotransformation, and elimination, thereby also affecting requirements for drug dosing and potentially altering the susceptibility of pregnant women to drug toxicity.[1, 2] During pregnancy, gastrointestinal transit time becomes prolonged; body water and fat increase throughout gestation and are accompanied by increases in cardiac output, ventilation, and liver and renal blood flow; plasma protein concentrations decrease; renal sodium reabsorption increases; and changes occur in cellular transporters and drug metabolizing enzymes in the liver and intestine. Placental transport of drugs, compartmentalization of drugs in the embryo/fetus and placenta, biotransformation of drugs by the fetus and placenta, and elimination of drugs by the fetus also can affect drug pharmacokinetics (PKs) in the pregnant woman.

Currently available data on the PKs of antiretroviral agents in pregnancy are summarized in Table 5. In general, the PKs of nucleoside reverse transcriptase inhibitors and non-nucleoside reverse transcriptase inhibitors are similar in pregnant and non-pregnant women, whereas protease inhibitor (PI) PKs are more variable, particularly in later pregnancy. Current data suggest that with standard adult dosing, plasma concentrations of lopinavir/ritonavir, atazanavir, darunavir, and nelfinavir are reduced during the second and/or third trimesters (see Table 5). The need for a dose adjustment depends on the PI, an individual patient's treatment experience, and use (if any) of concomitant medications with potential for drug interactions.[3-10]

References

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