untransformed delavirdine (ViiV Healthcare, product information, 2012).

5e. Drug interactions

Because delavirdine inhibits the cytochrome P-450 enzyme system, it has numerous and in some instances complex interactions with a variety of drugs that are metabolized by those enzymes. Drug interactions of delavirdine are summarized in Table 237.2 and Table 237.3.

ANTIRETROVIRAL DRUGS

Phase I studies showed that there was no apparent pharmacokinetic interaction between delavirdine and zidovudine (ViiV Healthcare, product information, 2012). Aside from the issue of oral absorption when delavirdine and didanosine are administered simultaneously, there does not appear to be an interaction between these drugs either. Studies of the interaction of delavirdine with other nucleoside or nucleotide analog reverse transcriptase inhibitors have not been conducted, although it seems likely that the interactions will be minimal.

Delavirdine probably increases plasma concentrations of most protease inhibitors (Harris *et al.*, 2002). Co-administration of delavirdine resulted in a 44% increase in the AUC of indinavir and some increase in $t_{½}$ with no effect on delavirdine pharmacokinetics (Ferry *et al.*, 1998). In a study by Kuritzkes *et al.* (2000) in highly drug-experienced patients, switching from a zidovudine–lamivudine–indinavir regimen to a zidovudine–delavirdine–indinavir combination markedly improved virologic outcomes (plasma HIV-1 RNA concentrations were ≤ 200 copies/ml in 48% of patients receiving the lamivudine combination and 83% in those receiving delavirdine, $p = 0.007$. Steady-state plasma indinavir levels were higher among patients in the delavirdine arm than among those in the lamivudine arm and, perhaps as a consequence, hyperbilirubinemia was also more common in the delavirdine arm than in the lamivudine arm. These investigators concluded that the reason for the better outcome in the delavirdine group was primarily its effect on plasma indinavir concentrations, not its antiviral effects *per se*.

A similar study in a busy New York City private practice also showed that adding delavirdine to a failing indinavir-based regimen (combined with two nucleoside analog reverse

Table 237.2. Pharmacokinetic variables for drugs co-administered with delavirdine.

Co-administered drug	Dose of co-administered drug	Dose of delavirdine	No. of subjects	% Change in pharmacokinetic variables of co-administered drug (90% CI)		
				C_{max}	AUC	C_{min}
HIV protease inhibitors						
Indinavir	400 mg tid × 7 days	400 mg tid × 7 days	28	↓ 36[a] (↓ 52–↓ 14)	↔[a]	↑ 118[a] (↑ 16–↑ 312)
	600 mg tid × days	400 mg tid × 7 days	28	↔	↑53[a] (↑ 7–↑120)	↑ 298[a] (104–↑ 678)
Nelfinavir[b]	750 mg tid × 14 days	400 mg tid × 7 days	12	↑ 88 (↑ 66–↑ 113)	↑ 107 (↑ 83–↑ 135)	↑ 136 (↑ 103–↑ 175)
Saquinavir	Soft gel capsule 1000 mg tid	400 mg tid × 28 days	20	↑ 98[c] (↑ 4–↑ 277)	↑ 121[c] (↑14–↑ 340)	↑ 199[c] (↑ 37–↑ 553)
Nucleoside reverse transcriptase inhibitors						
Didanosine (buffered tablets)	125 or 250 mg bid × 28 days	400 mg tid × 28 days	9	↓ 20[d] (↓ 44–↑ 15)	↓ 21[d] (↓ 40–↑ 5)	—
Zidovudine	200 mg tid for > 38 days	100 mg qid to 400 mg tid for 8–10 days	34	↔	↔	—
Anti-infective agents						
Clarithromycin	500 mg bid × 15 days	300 mg tid × 30 days	6	—	↑ 100	—
Rifabutin	300 mg qd for 15–99 days	400–1000 mg tid for 45–129 days	5	↑ 128 (↑ 71–↑ 203)	↑ 230 (↑ 119–↑ 396)	↑ 452 (↑ 246–↑ 781)

[a]Relative to indinavir 800 mg three times a day without delavirdine.

[b]Plasma concentrations of the nelfinavir-active metabolite (nelfinavir hydroxyl-*t*-butylamide) were significantly reduced by delavirdine, which is more than compensated for by increased nelfinavir concentration.

[c]Saquinavir soft gel capsule 1000 mg three times a day plus delavirdine 400 mg three times a day relative to saquinavir soft gel capsule 1200 mg three times a day without delavirdine.

[d]Delavirdine taken with didanosine (buffered tablets) relative to dose of delavirdine and didanosine (buffered tablets) separated by at least 1 hour.

Abbreviations: CI: confidence interval; C_{max}: maximum concentration; AUC: area-under-the-concentration-time curve; C_{min}: minimum concentration; ↑: increase; ↓: decrease; ↔: no significant change; —: no change.

Source: Data from ViiV Healthcare, product information (2008).