

Table 219.8. Pharmacokinetic variables of foscarnet in patients with normal renal function.

Dose (mg/kg)	Frequency	Duration	C _{max} (μM) ± SD	C _{min} (μM) ± SD	Steady-state (μM) ^a	t _{1/2} (h) ± SD	AUC ₀₋₂₄ (μM/min/kg) ± SD	V _d (l/kg)	Reference
90	Once	Once	990–5920		2556 ± 1334				Hengge <i>et al.</i> (1993)
230	Daily	≥ 10 days			75–529				Sjovall <i>et al.</i> (1988)
90	Every 12 hours	14 days	605 ± 118	52–59	218 ± 60				Taburet <i>et al.</i> (1992)
90	Every 12 hours	≥ 21 days	648 ± 124	44 ± 18		2.8 ± 0.5	5003 ± 1041	0.42	Castelli <i>et al.</i> (1997)
60	every 8 hours	≥ 21 days	619 ± 118	66 ± 27		2.4 ± 0.5	5138 ± 893	0.46	Castelli <i>et al.</i> , (1997)

^a1 μM is approximately equal to 0.3 μg/ml.

Abbreviations: C_{max}: maximum concentration; SD: standard deviation; C_{min}: minimum concentration; t_{1/2}: half-life; AUC: area-under-the-concentration-time curve; V_d: volume of distribution.

Table 219.9. Pharmacokinetic variables of intermittent infusion of foscarneta.

Subject no.	Concentration of foscarnet in plasma (μM) ^a				Plasma clearance (ml/min/kg)		Plasma half-life (hours)	Volume of distribution (l)
	Day 3		Day 14		Day 3	Day 14	Day 14	Day 14
	Peak	Trough	Peak	Trough				
1	382	63	506	101	2.6	1.9	3.7	0.60
2	306	62	272	57	3.6	3.6	6.6	2.00
3	544	98	608	139	1.1	1.1	3.5	0.34
4	720	117	639	225	1.1	1.1	4.9	0.45
5	368	91	348	92	1.9	1.9	5.7	0.96
6	876	116	699	121	1.5	1.5	3.4	0.44
7	520	147	493	199	0.9	0.9	5.0	0.37
8	359	86	395	75	1.7	1.7	3.3	0.49
Mean	509	98	495	126	1.7	1.7	4.5	0.74
Standard error	71	10	57	21	0.2	0.3	0.4	0.21

^aFoscarnet was given at a dose of 60 mg/kg every 8 hours, and plasma samples were taken at relevant time points for foscarnet concentrations as assessed by reverse-phase liquid chromatography. 1 μM is approximately equal to 0.3 μg/ml.

Source: Adapted with permission from Aweeka *et al.* (1989).

et al., 1993). During continuous administration of 230 mg/kg daily for 10–21 days, steady-state concentrations of foscarnet in plasma ranged between 75 and 529 μM (Sjovall *et al.*, 1988; Sjovall *et al.*, 1989; Fanning *et al.*, 1990). Steady-state concentrations of foscarnet during continuous intravenous administration are similar to those achieved with intermittent infusions.

In a study of HIV-infected patients with CMV disease who received 90 mg/kg of foscarnet twice daily by intravenous infusion for 14 days, the mean peak and trough levels (± SD) were 605 ± 118 and 52 ± 59 μM, respectively (Taburet

et al., 1992). The steady-state concentration of foscarnet in plasma was 218 ± 86 μM. In this same study, the plasma half-life of foscarnet was 3.4 hours. Owing to this relatively short half-life, there was no accumulation of the drug in plasma.

Aweeka and colleagues (1989) conducted a rigorous study of the pharmacokinetics of intravenous foscarnet in HIV-infected patients being treated for CMV retinitis with an induction dose of 60 mg/kg given every 8 hour. Kidney function did not change during the 2 weeks of study. Foscarnet maximum concentration (C_{max}) on day 3 varied nearly three-fold between 306 and 876 μM, and the C_{max} values were virtually unchanged on day 14, varying between 272 and 699 μM (see Table 219.9). The mean plasma half-life (t_{1/2}) of foscarnet was 4.5 hours and the mean volume of distribution was 0.74 l/kg. The plasma clearance rates observed by Aweeka *et al.* (1989) were virtually the same as that reported by Castelli *et al.* (1997) in a study comparing twice-daily with thrice-daily foscarnet infusions (see Tables 219.8 and 219.9); the mean plasma half-life of foscarnet observed in the Castelli study was 2–3 hours, whereas it was 4.5 hours in the Aweeka report. Dieterich and colleagues (1997) found that foscarnet pharmacokinetics in HIV-infected patients being treated for CMV gastrointestinal disease were similar to that found by

Table 219.10. Effects of renal dysfunction on foscarnet pharmacokinetic variables.

	Change in foscarnet variables with decreasing renal function			
Creatinine clearance (ml/minute)	> 80	50–80	25–49	10–24
Foscarnet clearance (ml/min/kg)	2.1	1.3	0.5	0.4
Foscarnet half-life (hours) mean (SD)	1.9 (0.1)	3.4 (0.9)	13 (4)	25 (19)