Table 219.7. Foscarnet therapy guidelines for patients with renal dysfunction.

A. Induction

CrCl (ml/min/kg)	HSV equivalent to		CMV equivalent to	
	80 mg/kg/day total (40 mg/kg every 12 hours)	120 mg/kg/day total (40 mg/kg every 8 hours)	180 mg/kg/day total (60 mg/kg every 8 hours)	180 mg/kg/day total (90 mg/kg every 12 hours)
> 1.4	40 every 12 hours	40 every 8 hours	60 every 8 hours	90 every 12 hours
> 1.0–1.4	30 every 12 hours	30 every 8 hours	45 every 8 hours	70 every 12 hours
> 0.8–1.0	20 every 12 hours	35 every 12 hours	50 every 12 hours	50 every 12 hours
> 0.6–0.8	35 every 24 hours	25 every 12 hours	40 every 12 hours	80 every 24 hours
> 0.5–0.6	25 every 24 hours	40 every 24 hours	60 every 24 hours	60 every 24 hours
> 0.4–0.5	20 every 24 hours	35 every 24 hours	50 every 24 hours	50 every 24 hours
< 0.4	Not recommended	Not recommended	Not recommended	Not recommended

B. Maintenance

CrCl (ml/min/kg)	CMV equivalent to	
	90 mg/kg/day (once daily)	120 mg/kg/day (once daily)
> 1.4	90 every 24 hours	120 every 24 hours
> 1.0–1.4	70 every 24 hours	90 every 24 hours
> 0.8–1.0	50 every 24 hours	65 every 24 hours
> 0.6–0.8	80 every 48 hours	105 every 48 hours
> 0.5–0.6	60 every 48 hours	80 every 48 hours
≥ 0.4–0.5	50 every 48 hours	65 every 48 hours
< 0.4	Not recommended	Not recommended

Abbreviations: CrCl: creatine clearance; HSV: herpes simpled virus; CMV: cytomegalovirus.
Source: Data from Cinigen Healthcare (2014).

clearance of foscarnet by hemodialysis was about 89 ml/minute. For patients undergoing foscarnet induction and receiving hemodialysis, the recommended dose is 50 mg/kg once daily; for maintenance therapy, the dose is 65 mg/kg once every 48 hours (both dosed after dialysis). Foscarnet is not recommended for use in patients undergoing continuous ambulatory peritoneal dialysis (CAPD) by some authors (Gilbert *et al.*, 2007), whereas others suggest a similar dose to that used for patients with a glomerular filtration rate (GFR) < 10 ml/minute (Aronoff *et al.*, 1999; see section 5d, Excretion).

PATIENTS WITH IMPAIRED HEPATIC FUNCTION

Because foscarnet is exclusively excreted by the kidneys, no adjustment needs to be made in the presence of hepatic insufficiency, although patients with severe liver disease can develop renal insufficiency, which would mandate dose adjustment.

THE ELDERLY

No studies of the efficacy or safety of foscarnet in patients over age 65 years have been conducted, although the pattern of efficacy and safety observed in patients of that age who have been treated is consistent with that seen in younger patients (Clinigen Healthcare, 2014). However, as elderly individuals may have underlying renal insufficiency requiring dosage adjustment, tests of renal function with dose adjustments as necessary should be conducted frequently.

5. PHARMACOKINETICS AND PHARMACODYNAMICS

5a. Bioavailability

Foscarnet is very poorly absorbed by mouth, and the doses required to overcome the poor oral absorption are also poorly tolerated. Mean bioavailability by the oral route in six asymptomatic HIV-infected subjects was between 7% and 10%; reducing gastric acidity (which causes foscarnet to decompose) with ranitidine increased absorption to only 10–17% (Barditch-Crovo *et al.*, 1998). The blood levels achieved in these studies of oral dosing were mostly below the limit of detection of the assay system (33 μM); even after blocking gastric acidity with ranitidine only 8 of 30 plasma samples tested showed detectable foscarnet.

The pharmacokinetics of foscarnet after intravenous administration has been found to vary widely between patients (Lietman, 1992; Taburet *et al.*, 1992; see Tables 219.8, 219.9, and 219.10). The variation in plasma levels of foscarnet may be partly attributed to interactions between plasma phosphate and the drug, resulting in variations in their sequestration in bone (Sjovall *et al.*, 1989; Wagstaff and Bryson, 1994). After a single infusion of foscarnet at a dose of 90 mg/kg, the plasma concentrations varied from 297 to 1775 μg/ml (990–5920 μM) with a mean (± SD) of 766 ± 400 μg/ml (Hengge *et*