Table 219.1. Viruses susceptible to clinically achievable concentrations of foscarnet.

Virus	IC_{50} (μM)	References
HSV-1 or -2	10–130	Package Insert, Foscavir
	10–45	Helgstrand *et al.* (1978); Eriksson and Oberg (1979); Ostrander and Cheng (1980)
Aciclovir-resistant HSV due to thymidine kinase deficiency	67	Package Insert, Foscavir
Varicella-zoster virus	42–85	Andrei *et al.* (1995)
Cytomegalovirus	50–800; mean 269	Package Insert, Foscavir
	34	Eriksson and Schinazi (1989)
	102–130	Wahren and Oberg (1980); Manischewitz *et al.* (1990)
	6–55	Wahren and Oberg (1980); Neyts *et al.* (1991); Andrei *et al.* (1991)
	108–270	Oberg (1989); Manischewitz *et al.* (1990); Gerna *et al.* (1994)
Epstein-Barr virus	47	Ballout *et al.* (2007)
HHV-6	4–15	De Clercq *et al.* (2001)
HHV-7	10–25	De Clercq *et al.* (2001)
HHV-8 (Kaposi's sarcoma–associated herpesvirus)	120	De Clercq *et al.* (2001)
	80–100	Kedes and Ganem (1997)
	97	Medveczky *et al.* (1997)
HIV	< 2	Sarin *et al.* (1985)
	10–25	Sandstrom *et al.* (1985); Eriksson and Schinazi (1989); Koshida *et al.* (1989)
	30	Cox *et al.* (1994)
Human hepatitis B virus	10–100	Oberg (1983)

Abbreviations: IC_{50}: half-maximal inhibitory concentration; HSV: herpes simplex virus; HHV: human herpesvirus.

Manischewitz *et al.*, 1990; Gerna *et al.*, 1994; Chrisp and Clissold, 1991; Wagstaff and Bryson, 1994).

HERPES SIMPLEX VIRUSES

Foscarnet inhibits HSV-1 and 2 with EC_{50} values of 0.4–3.5 μM for HSV-1 and 0.6–22 μM for HSV-2 (Helgstrand *et al.*, 1978; Eriksson and Oberg, 1979; Ostrander and Cheng, 1980).

VARICELLA-ZOSTER VIRUS

The IC_{50} of foscarnet required to inhibit the DNA polymerase of VZV is 0.4 μM (Oberg, 1989). Foscarnet was active against virtually all strains of VZV tested (Andrei *et al.*, 1995).

OTHER HUMAN HERPESVIRUSES

In vitro, foscarnet inhibits all human herpesviruses that have been tested, including EBV, HHV-6, and HHV-8. Foscarnet, cidofovir, and ganciclovir were all active against EBV, at EC_{50} values of 14, 0.29, and 0.28 μg/ml, respectively (approx. 46, 1 and 1 μM) (Ballout *et al.*, 2007).

Both foscarnet and cidofovir inhibited HHV-6 type A replication in glial cells, whereas aciclovir and ganciclovir were inactive (Akhyani *et al.*, 2006). In a range of antiviral drugs including foscarnet (the others being aciclovir, penciclovir, ganciclovir, brivudin, and cidofovir), foscarnet was the most active against HHV-6 and was also active against HHV-7 and HHV-8 (De Clercq *et al.*, 2001). Some support for the *in vivo* activity of foscarnet against HHV-6 comes from two reports; one of a patient with meningitis with bilateral uveitis due to HHV-6 who recovered after foscarnet therapy (Maslin *et al.*, 2007) and another case of a patient immunosuppressed for a hematopoietic stem cell transplant with a systemic HHV-6 infection that was rapidly controlled with foscarnet (Gregg *et al.*, 2014; see section 7, Clinical uses of the drug).

Using a cell line latently infected with HHV-8, Kedes and Ganem (1997) assessed the ability of foscarnet to block production of the virus after active replication was induced by phorbol esters. HHV-8 was susceptible to foscarnet, ganciclovir, and cidofovir, with EC_{50} values of 80–100, 2.7–4.0, and 0.5–1.0 μM, respectively. Another study also evaluated foscarnet, ganciclovir, and cidofovir for their inhibitory activity against HHV-8 in a lymphoma cell line; EC_{50} values were 97, 5.1, and 0.05 μM, respectively, but none of these drugs eliminated HHV-8 episomes (Medveczky *et al.*, 1997). Foscarnet inhibited production of HHV-8 infection of primary microvascular endothelial cells, but only interferon-alpha inhibited expansion of latently infected cells. Overall, interferon-alpha was thought to be a more effective antiviral strategy for HHV-8 infection than an antiviral drug (Krug *et al.*, 2004). However, the *in vivo* evidence for the activity of foscarnet against HHV-8 is decidedly mixed (see section 7, Clinical uses of the drug).

HUMAN IMMUNODEFICIENCY VIRUS

Foscarnet inhibits HIV-1 and -2 and SIV (Sarin *et al.*, 1985; Vrang *et al.*, 1988). The concentration of foscarnet required to inhibit the HIV-1 reverse transcriptase by 50% was < 2 μM (Sarin *et al.*, 1985), and complete inhibition of enzyme activity