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Pharmacokinetics of Penciclovir following Oral Famciclovir in Subjects with Mild Renal Impairment.
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Famciclovir (FCV) is the oral form of a new, potent and selective antiherpes drug, penciclovir (PCV), which is eliminated predominantly unchanged by the renal route. Therefore, a retrospective review was performed of PK data from 3 clinical studies in which subjects had a mild degree of renal impairment at baseline, assessed by creatinine clearance (CrCl) estimated from serum creatinine values. In one study, 18 healthy elderly subjects (mean age 71 years, range 65-79) received a single dose of FCV 750 mg; in another, 6 subjects with mild renal impairment (mean age 39 years, range 25-50) received a single dose of FCV 500 mg and in a third, 7 subjects with herpes zoster (mean age 58 years, range 47 -65) received 7 days dosing with FCV 500 mg tid. Since the PK of PCV from FCV is dose linear over the range 125 - 750mg, PK data for PCV following dosing with FCV in these studies was dose-normalised to 500 mg (where appropriate) and was compared with historical data obtained from all single dose studies conducted in normal volunteers.

Population	N+	Range of Cr Cl ($ml/min/1.73m^2$)	Mean Cmax (range) (ug/ml)	Mean AUC (range) (ug.h/ml)
Elderly volunteers	18	39-68	3.56* (2.2-4.9)	12.5* (9.0-17.7)
Mild renal imp	6	60-77	3.3 (2.0-4.4)	8.8 (5.7-10.9)
Herpes zoster	7	56-64	3.4 (3.1-4.9)	10.5 (9.7-13.9)
Healthy young volunteers	223	>= 80	+3.3 (1.3-6.3)	9.0 (3.9-18.0)

* dose-normalised to a FCV dose of 500mg +N = 160

Systemic exposure to PCV following dosing with FCV in subjects with a mild degree of renal impairment as measured by Cmax & AUC is comparable to young healthy volunteers. Consistent with this, FCV was well-tolerated in all subjects. In conclusion, there are no PK or safety grounds to reduce either dose or dosing frequency in patients with a mild degree of renal impairment.

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Tissue Distribution and Bioavailability of Cyclic HPMPC, an Intracellular Prodrug of HPMPC

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Cyclic HPMPC is an intracellular prodrug of HPMPC which has been shown to be less nephrotoxic after i.v. administration in preclinical toxicology studies. Tissue distribution studies in the rat comparing cyclic HPMPC to HPMPC showed an equivalent distribution of radiolabelled drug in all tissues except the kidney. Kidney levels were 14-fold greater after administration of HPMPC. The oral bioavailability of cyclic HPMPC in rats was highly variable (2-26%) and in monkeys and dogs it was 16±4.5 % and 22±4 %, respectively. The moderate oral bioavailability of cyclic HPMPC was unexpected based on *in vitro* permeability measurements and potentially indicates an active transport process across the intestinal mucosa.