Clinical Pharmacokinetics and Pharmacodynamics of Cefiderocol

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Supplement

Supplemental Table 1. Summary of ratios of PK parameters for furosemide, metformin and rosuvastatin with and without cefiderocol [25]

Parameter	Furosemide and cefiderocol/ furosemide	Metformin and cefiderocol/ metformin	Rosuvastatin and cefiderocol/ rosuvastatin
C_{max}	1.00 (0.709, 1.42)	1.09 (0.922, 1.28)	1.28 (1.12, 1.46)
$AUC_{0\text{-last}}$	1.01 (0.878, 1.15)	1.03 (0.934, 1.15)	1.24 (1.10, 1.40)
$AUC_{0\text{-inf}}$	0.917 (0.728, 1.16)	0.932 (0.725 1.20)	1.21 (1.08, 1.35)
$t_{1/2}$,z	1.25 (0.97, 1.59)	0.932 (0.725, 1.20)	1.19 (0.842, 1.67)

The geometric least squares mean ratios (90% confidence intervals) are shown for a selection of PK parameters for drugs administered alone versus in combination with cefiderocol. C_{max}, maximum plasma concentration; $AUC_{0\text{-last}}$ (mg·h/L), area under plasma concentration-time curve from zero to the time of the last quantifiable concentration; $AUC_{0\text{-inf}}$ (mg·h/L), area under plasma concentration-time curve from zero to infinity; $t_{1/2,z}$ (h), terminal elimination half-life; t_{max} (h), time to $C_{max;}$ CV, coefficient of variation. Based on [25].

Supplemental Table 2. Probability of target attainment for 75% and 100% fT>MIC by infection and renal group [27]

			Probability of target attainment for 75% fT>MIC			Probability of target attainment for 100% fT>MIC		
Renal group and infection	**CRCL (mL/min)**	**Dose (3-h infusion)**	**PTA (%) for MIC (mg/L) of:**			**PTA (%) for MIC (mg/L) of:**		
			1 (mg/L)	**2 (mg/L)**	**4 (mg/L)**	**1 (mg/L)**	**2 (mg/L)**	**4 (mg/L)**
Pneumonia patients								
Augmented	≥ 120*	2 g q6h	100	100	99.7	100	99.7	95.9
Normal	90 to < 120	2 g q8h	100	99.9	98.9	99.9	98.3	91.2
Mild	60 to < 90	2 g q8h	100	100	99.8	99.9	99.7	98.2
Moderate	30 to < 60	1.5 g q8h	100	100	99.9	100	100	99.5
Severe	15 to < 30	1 g q8h	100	100	100	100	100	100
ESRD	5 to < 15	0.75 g q12h	100	100	100	100	100	100
BSI/sepsis patients								
Augmented	≥ 120*	2 g q6h	100	100	99.4	100	99.4	93.6
Normal	90 to < 120	2 g q8h	100	99.9	97.3	99.5	96.2	85.8
Mild	60 to < 90	2 g q8h	100	99.9	99.6	99.8	99.4	96.0
Moderate	30 to < 60	1.5 g q8h	100	100	99.9	100	99.9	98.7
Severe	15 to < 30	1 g q8h	100	100	100	100	100	100
ESRD	5 to < 15	0.75 g q12h	100	100	100	100	100	100
cUTI patients								
Augmented	≥ 120*	2 g q6h	100	100	99.9	100	100	98.0
Normal	90 to < 120	2 g q8h	100	100	99.6	99.9	99.4	95.1
Mild	60 to < 90	2 g q8h	100	100	99.8	100	99.8	98.9
Moderate	30 to < 60	1.5 g q8h	100	100	100	100	100	99.8
Severe	15 to < 30	1 g q8h	100	100	100	100	100	100
ESRD	5 to < 15	0.75 g q12h	100	100	100	100	100	100

*Augmented renal clearance (120 to <150 = 50%, >150 = 50%), CRCL; Creatinine clearance, ESRD; End stage renal disease. Shown are the probabilities of target attainment (PTA) for different minimum inhibitory concentrations (MIC) and patient groups, including patients with pneumonia, blood stream infections (BSI) or sepsis and with complicated urinary tract infection (cUTI). Based on [27].