

## Supplementary data

**Table S1.** Comparison (geometric mean ratio) of estimated pharmacokinetic parameters of daptomycin: day 1 versus day 7

	Mean ratio of day 1 versus day 7 (95% CI)	
	daptomycin 4 mg/kg	daptomycin 6 mg/kg
$AUC_{0-\tau}$	1.21 (0.99–1.49)	1.17 (1.06–1.28)
CL	0.97 (0.79–1.2)	0.99 (0.9–1.08)
$C_{\max}$	1.1 (0.93–1.31)	0.94 (0.81–1.1)
$Ae_{0-\tau}$	1.26 (0.99–1.61)	1.17 (0.91–1.49)

$Ae_{0-\tau}$ , cumulative amount of unchanged daptomycin excreted in urine;  $AUC_{0-\tau}$ , area under the plasma concentration–time curve from time zero to 24 h; CI, confidence interval.

**Table S2.** Model predicted population pharmacokinetic parameters of daptomycin following a single dose and multiple doses of the daptomycin 2 min iv injection or 30 min iv infusion

	Population mean ( $\theta$ )	Standard error of $\theta$ estimates	Inter-individual variability ( $\eta$ ), CV	Standard error of $\eta$ estimates
CL (L/min)	0.0110	0.000301	0.0196	0.00731
V1 (or $V_c$ ) (L)	4.79	0.232	0.0474	0.0154
Q (or $CL_d$ ) (L/min)	0.0428	0.00516	NE	NE
V2 (or $V_t$ ) (L)	2.98	0.133	0.0162	0.0105
D1 (infusion) (min)	28.0	0.648	NE	NE
D1 (injection) (min)	2.35	0.175	NE	NE
Residual variability (CV)	0.0175	0.00288	NE	NE

CV, coefficient of variance; D1 (infusion), model-estimated duration of zero-order input for 30 min iv infusion; D1 (injection), model-estimated duration of zero-order input for 2 min iv injection; NE, not estimated; V1 (or  $V_c$ ), volume of the central compartment; Q (or  $CL_d$ ), clearance between central and tissue compartments; V2 (or  $V_t$ ), peripheral volume of distribution of the tissue compartment.

An inter-occasion variance was included for CL ( $\eta=0.00253$ ) and variance ( $\eta$ ) of V1 for the injection regimen was 0.0612.

**Figure S1.** Diagnostic plots for the daptomycin population pharmacokinetic model.

Observed versus individual predicted daptomycin concentrations in plasma (left-hand panel), observed versus population predicted daptomycin concentrations in plasma (middle panel) and weighted residuals versus population predicted daptomycin concentrations in plasma (right-hand panel) are shown. Circles represent individual data points. Broken lines represent regression lines. Continuous lines represent unity.

