

Supplemental material

Amikacin initial dose in critically ill patients: a nonparametric approach to optimize a priori PK/PD target attainments in individual patients

Figure S1

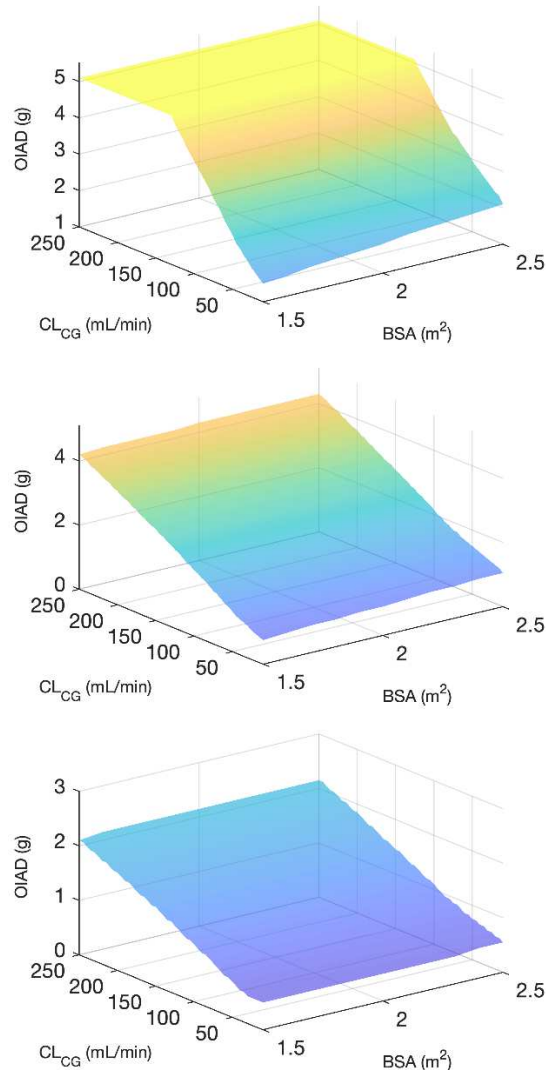


Figure S1: Optimal initial amikacin dose (OIAD) targeting $AUC_{0-24h}/MIC \geq 75$ as a function of body surface area and creatinine clearance estimated by Cockcroft & Gault formula, for different MIC values.

Abbreviations: Top panel, MIC = 8 mg/L; center panel, MIC = 4 mg/L, bottom panel, MIC = 2 mg/L. BSA, Body Surface Area; CL_{CG}, Creatinine clearance estimated by Cockcroft & Gault equation; MIC, bacterial minimal inhibitory concentration; $AUC_{0-24h}/MIC \geq 75$, amikacin daily area under the curve over MIC ratio ≥ 75 .

Note that the maximal dose was capped to 5 g.

Table S1: Optimal initial amikacin dosing recommendations based on CLCG and BSA with associated efficacy and safety target attainment rates assuming a MIC value of 8 mg/L.

Abbreviations : BSA, Body Surface Area; CLCG, Creatinine clearance estimated by Cockcroft & Gault equation; MIC, bacterial minimal inhibitory concentration; Cmax/MIC ≥ 8, probability of amikacin maximal plasma concentration over MIC ratio ≥ 8 , AUC/MIC ≥ 75, probability of amikacin daily area under the curve over MIC ratio ≥ 75; Cmin 24 ≤ 2.5mg/L, amikacin plasma concentration at 24h ≤ 2.5 mg/L probability; Cmin 48, amikacin plasma concentration at 48h ≤ 2.5 mg/L probability.

The maximal dose was capped to 5 g.

	BSA (m2)	1.5		1.6		1.7		1.8		1.9	
CLCG (mL/min)	Targeted index	Cmax/MIC ≥ 8	AUC/MIC ≥ 75	Cmax/MIC ≥ 8	AUC/MIC ≥ 75	Cmax/MIC ≥ 8	AUC/MIC ≥ 75	Cmax/MIC ≥ 8	AUC/MIC ≥ 75	Cmax/MIC ≥ 8	AUC/MIC ≥ 75
10	Optimal dose (g)	2.4	1.5	2.55	1.55	2.7	1.65	2.85	1.7	3	1.75
	Target attainment (%)	92.01	90.27	92.01	90.27	92.01	92.39	92.01	92.39	92.01	91.47
	Cmin 24 ≤ 2.5 mg/L (%)	0	0	0	0	0	0	0	0	0	0
	Cmin 48 ≤ 2.5 mg/L (%)	0	1.81	0	1.81	0	1.81	0	1.81	0	1.81
20	Optimal dose (g)	2.45	1.7	2.6	1.75	2.75	1.8	2.9	1.9	3.05	1.95
	Target attainment (%)	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27
	Cmin 24 ≤ 2.5 mg/L (%)	1.81	1.81	1.81	1.81	0	1.81	0	1.81	0	1.81
	Cmin 48 ≤ 2.5 mg/L (%)	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81
30	Optimal dose (g)	2.45	1.95	2.6	2	2.75	2.05	2.9	2.1	3.1	2.15
	Target attainment (%)	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27
	Cmin 24 ≤ 2.5 mg/L (%)	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81
	Cmin 48 ≤ 2.5 mg/L (%)	6.84	10.29	6.84	10.29	3.93	10.29	3.93	10.29	1.81	10.29
40	Optimal dose (g)	2.5	2.2	2.65	2.25	2.8	2.3	2.95	2.35	3.1	2.4
	Target attainment (%)	92.01	92.98	92.01	92.98	92.01	90.27	92.01	90.27	92.01	90.27
	Cmin 24 ≤ 2.5 mg/L (%)	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81
	Cmin 48 ≤ 2.5 mg/L (%)	13.31	18.18	13.31	17.27	10.29	13.31	10.29	13.31	10.29	13.31

50	Optimal dose (g)	2.55	2.5	2.7	2.5	2.85	2.55	3	2.6	3.15	2.65
	Target attainment (%)	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08	92.01	92.98
	Cmin 24 ≤ 2.5 mg/L (%)	4.72	4.72	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81
	Cmin 48 ≤ 2.5 mg/L (%)	44.42	53.17	22.64	44.42	18.18	44.42	17.27	22.64	15.09	18.18
60	Optimal dose (g)	2.55	2.8	2.7	2.85	2.85	2.85	3	2.9	3.2	2.9
	Target attainment (%)	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08
	Cmin 24 ≤ 2.5 mg/L (%)	10.29	10.29	10.29	6.84	4.72	4.72	4.72	4.72	1.81	4.72
	Cmin 48 ≤ 2.5 mg/L (%)	63.27	63.27	63.27	62.03	58.89	58.89	58.89	58.89	53.17	58.89
70	Optimal dose (g)	2.6	3.15	2.75	3.15	2.9	3.2	3.05	3.2	3.2	3.25
	Target attainment (%)	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08
	Cmin 24 ≤ 2.5 mg/L (%)	10.29	10.29	10.29	10.29	10.29	10.29	10.29	10.29	6.84	6.84
	Cmin 48 ≤ 2.5 mg/L (%)	64.62	63.27	64.62	63.27	63.27	63.27	63.27	63.27	63.27	63.27
80	Optimal dose (g)	2.65	3.5	2.8	3.5	2.95	3.5	3.1	3.55	3.25	3.55
	Target attainment (%)	92.01	92.25	92.01	92.25	92.01	90.08	92.01	90.08	92.01	90.08
	Cmin 24 ≤ 2.5 mg/L (%)	13.31	10.29	13.31	10.29	10.29	10.29	10.29	10.29	10.29	10.29
	Cmin 48 ≤ 2.5 mg/L (%)	74.15	64.62	64.62	64.62	64.62	63.27	64.62	63.27	63.27	63.27
90	Optimal dose (g)	2.65	3.8	2.8	3.8	2.95	3.85	3.1	3.85	3.25	3.85
	Target attainment (%)	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	90.08
	Cmin 24 ≤ 2.5 mg/L (%)	45.79	13.31	36.88	13.31	25.42	10.29	13.31	10.29	10.29	10.29
	Cmin 48 ≤ 2.5 mg/L (%)	76.6	64.62	74.15	64.62	74.15	64.62	70.44	64.62	64.62	64.62
100	Optimal dose (g)	2.7	4.1	2.85	4.15	3	4.15	3.15	4.15	3.3	4.2
	Target attainment (%)	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	59.22	15.09	57.95	13.31	45.79	13.31	38.28	13.31	35.09	10.29
	Cmin 48 ≤ 2.5 mg/L (%)	88.69	73.16	80.49	67.34	76.68	64.62	74.15	64.62	74.15	64.62
110	Optimal dose (g)	2.75	4.4	2.9	4.45	3.05	4.45	3.2	4.45	3.35	4.5
	Target attainment (%)	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	63.27	36.88	63.27	36.88	57.95	35.09	50.33	25.42	45.79	13.31

	Cmin 48 ≤ 2.5 mg/L (%)	92.99	74.15	88.69	74.15	87.77	74.15	80.49	74.15	78.04	70.44
120	Optimal dose (g)	2.75	4.75	2.9	4.75	3.05	4.75	3.2	4.8	3.35	4.8
	Target attainment (%)	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	63.27	53.51	63.27	48.06	63.27	42.6	61.09	36.88	57.95	35.09
	Cmin 48 ≤ 2.5 mg/L (%)	92.99	76.6	92.99	74.15	92.99	74.15	88.69	74.15	87.77	74.15
130	Optimal dose (g)	2.8	> 5	2.95	> 5	3.1	> 5	3.25	> 5	3.4	> 5
	Target attainment (%)	92.01	88.8	92.01	88.8	92.01	88.8	92.01	88.8	92.01	88.8
	Cmin 24 ≤ 2.5 mg/L (%)	64.62	60.13	63.27	56.71	63.27	56.71	63.27	49.08	62.36	45.79
	Cmin 48 ≤ 2.5 mg/L (%)	92.99	79.14	92.99	79.14	92.99	79.14	92.99	74.15	92.99	74.15
140	Optimal dose (g)	2.8	> 5	2.95	> 5	3.1	> 5	3.25	> 5	3.45	> 5
	Target attainment (%)	92.01	86.63	92.01	86.63	92.01	86.63	92.01	86.63	92.01	86.63
	Cmin 24 ≤ 2.5 mg/L (%)	70.44	60.13	64.62	60.13	64.62	59.22	63.27	57.95	63.27	57.95
	Cmin 48 ≤ 2.5 mg/L (%)	92.99	88.69	92.99	88.69	92.99	80.49	92.99	80.49	92.99	80.49
150	Optimal dose (g)	2.85	> 5	3	> 5	3.15	> 5	3.3	> 5	3.45	> 5
	Target attainment (%)	92.01	86.63	92.01	86.63	92.01	86.63	92.01	86.63	92.01	86.63
	Cmin 24 ≤ 2.5 mg/L (%)	70.44	63.27	70.44	63.27	70.44	63.27	64.62	59.22	64.62	59.22
	Cmin 48 ≤ 2.5 mg/L (%)	94.47	88.69	92.99	88.69	92.99	88.69	92.99	88.69	92.99	87.77
160	Optimal dose (g)	2.9	> 5	3.05	> 5	3.2	> 5	3.35	> 5	3.5	> 5
	Target attainment (%)	93.28	80.55	92.01	80.55	92.01	80.55	92.01	80.55	92.01	80.55
	Cmin 24 ≤ 2.5 mg/L (%)	71.44	63.27	70.44	63.27	70.44	63.27	70.44	63.27	64.62	63.27
	Cmin 48 ≤ 2.5 mg/L (%)	94.47	92.99	94.47	92.99	94.47	92.99	92.99	92.99	92.99	92.99
170	Optimal dose (g)	2.9	> 5	3.05	> 5	3.2	> 5	3.35	> 5	3.5	> 5
	Target attainment (%)	92.01	80.55	92.01	80.55	92.01	80.55	92.01	80.55	92.01	80.55
	Cmin 24 ≤ 2.5 mg/L (%)	78.44	63.27	71.44	63.27	70.44	63.27	70.44	63.27	70.44	63.27
	Cmin 48 ≤ 2.5 mg/L (%)	94.47	92.99	94.47	92.99	94.47	92.99	94.47	92.99	92.99	92.99
180	Optimal dose (g)	2.95	> 5	3.1	> 5	3.25	> 5	3.4	> 5	3.55	> 5
	Target attainment (%)	93.28	80.55	93.28	80.55	92.01	80.55	92.01	80.55	92.01	80.55

	Cmin 24 ≤ 2.5 mg/L (%)	80.97	70.44	78.44	70.44	71.44	64.62	70.44	63.27	70.44	63.27
	Cmin 48 ≤ 2.5 mg/L (%)	96.83	92.99	94.47	92.99	94.47	92.99	94.47	92.99	94.47	92.99
190	Optimal dose (g)	3	> 5	3.15	> 5	3.3	> 5	3.45	> 5	3.6	> 5
	Target attainment (%)	91.47	80.55	93.28	80.55	93.28	80.55	93.28	80.55	92.01	80.55
	Cmin 24 ≤ 2.5 mg/L (%)	85.32	70.44	78.44	70.44	78.44	70.44	77.08	70.44	70.44	64.62
	Cmin 48 ≤ 2.5 mg/L (%)	96.83	92.99	96.83	92.99	94.47	92.99	94.47	92.99	94.47	92.99
200	Optimal dose (g)	3	> 5	3.15	> 5	3.3	> 5	3.45	> 5	3.6	> 5
	Target attainment (%)	91.47	80.55	91.47	80.55	93.28	80.55	92.01	80.55	92.01	80.55
	Cmin 24 ≤ 2.5 mg/L (%)	92.07	71.44	83.68	71.44	78.44	70.44	78.44	70.44	77.08	70.44
	Cmin 48 ≤ 2.5 mg/L (%)	96.83	94.47	96.83	94.47	96.83	92.99	94.47	92.99	94.47	92.99
210	Optimal dose (g)	3.05	> 5	3.2	> 5	3.35	> 5	3.5	> 5	3.65	> 5
	Target attainment (%)	91.47	100	91.47	100	93.28	100	93.28	72.39	93.28	69.1
	Cmin 24 ≤ 2.5 mg/L (%)	92.07	72.79	92.07	71.44	83.68	71.44	78.44	70.44	78.44	70.44
	Cmin 48 ≤ 2.5 mg/L (%)	96.83	94.47	96.83	94.47	96.83	94.47	96.83	94.47	94.47	92.99
220	Optimal dose (g)	3.1	> 5	3.2	> 5	3.35	> 5	3.5	> 5	3.65	> 5
	Target attainment (%)	91.47	59.42	91.47	59.42	91.47	59.42	93.28	59.42	92.01	59.42
	Cmin 24 ≤ 2.5 mg/L (%)	92.07	77.01	92.07	74.47	89.62	72.79	80.97	71.44	78.44	71.44
	Cmin 48 ≤ 2.5 mg/L (%)	96.83	94.47	96.83	94.47	96.83	94.47	96.83	94.47	96.83	94.47
230	Optimal dose (g)	3.1	> 5	3.25	> 5	3.4	> 5	3.55	> 5	3.7	> 5
	Target attainment (%)	91.47	41.59	91.47	41.59	91.47	41.59	91.47	41.59	93.28	41.59
	Cmin 24 ≤ 2.5 mg/L (%)	92.07	83.68	92.07	80.97	92.07	78.44	89.62	78.44	80.97	73.12
	Cmin 48 ≤ 2.5 mg/L (%)	96.83	96.83	96.83	94.47	96.83	94.47	96.83	94.47	96.83	94.47
240	Optimal dose (g)	3.15	> 5	3.3	> 5	3.45	> 5	3.6	> 5	3.75	> 5
	Target attainment (%)	91.47	41.59	91.47	41.59	91.47	41.59	91.47	41.59	93.28	41.59
	Cmin 24 ≤ 2.5 mg/L (%)	92.99	87.77	92.07	83.68	92.07	80.97	92.07	78.44	87.99	78.44
	Cmin 48 ≤ 2.5 mg/L (%)	96.83	96.83	96.83	96.83	96.83	94.47	96.83	94.47	96.83	94.47
250	Optimal dose (g)	3.2	> 5	3.3	> 5	3.45	> 5	3.6	> 5	3.75	> 5

Target attainment (%)	92.39	41.59	91.47	41.59	91.47	41.59	91.47	41.59	91.47	41.59
Cmin 24 ≤ 2.5 mg/L (%)	92.99	92.07	92.99	92.07	92.07	83.68	92.07	80.97	89.62	78.44
Cmin 48 ≤ 2.5 mg/L (%)	96.83	96.83	96.83	96.83	96.83	96.83	96.83	96.83	96.83	94.47

Table S1 continued

CLCG (mL/min)	BSA (m ²) Targeted index	2		2.1		2.2		2.3		2.4		2.5	
		Cmax/MIC ≥ 8	AUC/MIC ≥ 75	Cmax/MIC ≥ 8	AUC/MIC ≥ 75	Cmax/MIC ≥ 8	AUC/MIC ≥ 75	Cmax/MIC ≥ 8	AUC/MIC ≥ 75	Cmax/MIC ≥ 8	AUC/MIC ≥ 75	Cmax/MIC ≥ 8	AUC/MIC ≥ 75
10	Optimal dose (g)	3.15	1.8	3.3	1.9	3.45	1.95	3.6	2	3.75	2.05	3.9	2.1
	Target attainment (%)	92.01	91.47	92.01	93.28	92.01	93.28	92.01	93.28	92.01	93.28	92.01	93.28
	Cmin 24 ≤ 2.5 mg/L (%)	0	0	0	0	0	0	0	0	0	0	0	0
	Cmin 48 ≤ 2.5 mg/L (%)	0	1.81	0	1.81	0	1.81	0	0	0	0	0	0
20	Optimal dose (g)	3.2	2	3.35	2.1	3.5	2.15	3.65	2.2	3.8	2.3	3.95	2.35
	Target attainment (%)	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27
	Cmin 24 ≤ 2.5 mg/L (%)	0	1.81	0	0	0	0	0	0	0	0	0	0
	Cmin 48 ≤ 2.5 mg/L (%)	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81
30	Optimal dose (g)	3.25	2.25	3.4	2.3	3.55	2.35	3.7	2.4	3.85	2.5	4	2.55
	Target attainment (%)	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27
	Cmin 24 ≤ 2.5 mg/L (%)	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81
	Cmin 48 ≤ 2.5 mg/L (%)	1.81	6.84	1.81	6.84	1.81	6.84	1.81	1.81	1.81	1.81	1.81	1.81
40	Optimal dose (g)	3.25	2.45	3.4	2.5	3.55	2.6	3.7	2.65	3.9	2.7	4.05	2.75
	Target attainment (%)	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27
	Cmin 24 ≤ 2.5 mg/L (%)	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81
	Cmin 48 ≤ 2.5 mg/L (%)	10.29	10.29	10.29	10.29	6.84	10.29	6.84	10.29	4.72	10.29	1.81	10.29
50	Optimal dose (g)	3.3	2.7	3.45	2.75	3.6	2.8	3.75	2.85	3.9	2.9	4.05	2.95

	Target attainment (%)	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27
	Cmin 24 ≤ 2.5 mg/L (%)	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81
	Cmin 48 ≤ 2.5 mg/L (%)	13.31	17.27	13.31	15.09	10.29	13.31	10.29	13.31	10.29	13.31	10.29	13.31
60	Optimal dose (g)	3.35	2.95	3.5	2.95	3.65	3.05	3.8	3.1	3.95	3.15	4.1	3.2
	Target attainment (%)	92.01	90.08	92.01	90.08	92.01	92.98	92.01	90.27	92.01	90.27	92.01	90.27
	Cmin 24 ≤ 2.5 mg/L (%)	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81
	Cmin 48 ≤ 2.5 mg/L (%)	44.42	58.89	17.27	58.89	15.09	43.15	13.31	39.05	13.31	36.88	13.31	36.88
70	Optimal dose (g)	3.35	3.25	3.5	3.25	3.65	3.3	3.8	3.3	3.95	3.35	4.1	3.45
	Target attainment (%)	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08	92.01	92.98
	Cmin 24 ≤ 2.5 mg/L (%)	4.72	4.72	4.72	4.72	1.81	4.72	1.81	4.72	1.81	1.81	1.81	1.81
	Cmin 48 ≤ 2.5 mg/L (%)	60.13	63.27	58.89	60.13	58.89	60.13	58.89	60.13	42.24	58.89	36.88	58.89
80	Optimal dose (g)	3.4	3.55	3.55	3.6	3.7	3.6	3.85	3.6	4	3.65	4.15	3.65
	Target attainment (%)	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08
	Cmin 24 ≤ 2.5 mg/L (%)	10.29	10.29	10.29	10.29	4.72	4.72	4.72	4.72	4.72	4.72	1.81	4.72
	Cmin 48 ≤ 2.5 mg/L (%)	63.27	63.27	63.27	63.27	63.27	63.27	60.13	63.27	60.13	63.27	60.13	60.13
90	Optimal dose (g)	3.4	3.9	3.6	3.9	3.75	3.9	3.9	3.95	4.05	3.95	4.2	3.95
	Target attainment (%)	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08
	Cmin 24 ≤ 2.5 mg/L (%)	10.29	10.29	10.29	10.29	10.29	10.29	10.29	10.29	4.72	8.17	4.72	4.72
	Cmin 48 ≤ 2.5 mg/L (%)	64.62	63.27	63.27	63.27	63.27	63.27	63.27	63.27	63.27	63.27	63.27	63.27
100	Optimal dose (g)	3.45	4.2	3.6	4.2	3.75	4.2	3.9	4.25	4.05	4.25	4.2	4.25
	Target attainment (%)	92.01	92.25	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08
	Cmin 24 ≤ 2.5 mg/L (%)	25.42	10.29	10.29	10.29	10.29	10.29	10.29	10.29	10.29	10.29	10.29	10.29
	Cmin 48 ≤ 2.5 mg/L (%)	71.44	64.62	70.44	64.62	64.62	64.62	64.62	63.27	63.27	63.27	63.27	63.27
110	Optimal dose (g)	3.5	4.5	3.65	4.5	3.8	4.55	3.95	4.55	4.1	4.55	4.25	4.6
	Target attainment (%)	92.01	92.25	92.01	92.25	92.01	92.25	92.01	90.08	92.01	90.08	92.01	90.08
	Cmin 24 ≤ 2.5 mg/L (%)	38.28	13.31	38.28	13.31	28.61	10.29	10.29	10.29	10.29	10.29	10.29	10.29
	Cmin 48 ≤ 2.5 mg/L (%)	74.15	70.44	71.44	70.44	71.44	64.62	70.44	64.62	70.44	64.62	64.62	64.62

120	Optimal dose (g)	3.5	4.8	3.65	4.8	3.8	4.85	3.95	4.85	4.1	4.85	4.3	4.9
	Target attainment (%)	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	90.08	92.01	90.08
	Cmin 24 ≤ 2.5 mg/L (%)	47.03	35.09	44	25.42	38.28	25.42	38.28	10.29	28.61	10.29	13.48	10.29
	Cmin 48 ≤ 2.5 mg/L (%)	82.17	71.44	78.04	71.44	74.15	70.44	71.44	70.44	71.44	70.44	70.44	70.44
130	Optimal dose (g)	3.55	> 5	3.7	> 5	3.85	> 5	4	> 5	4.15	> 5	4.3	> 5
	Target attainment (%)	92.01	88.8	92.01	88.8	92.01	86.63	92.01	86.63	92.01	86.63	92.01	86.63
	Cmin 24 ≤ 2.5 mg/L (%)	61.09	38.28	53.47	38.28	47.03	38.28	38.28	28.61	38.28	28.61	28.61	28.61
	Cmin 48 ≤ 2.5 mg/L (%)	87.77	74.15	87.77	74.15	86.13	71.44	79.72	71.44	75.5	71.44	71.44	71.44
140	Optimal dose (g)	3.6	> 5	3.75	> 5	3.9	> 5	4.05	> 5	4.2	> 5	4.35	> 5
	Target attainment (%)	92.01	86.63	92.01	86.63	92.01	86.63	92.01	86.63	92.01	86.63	92.01	86.63
	Cmin 24 ≤ 2.5 mg/L (%)	62.36	50.33	61.09	47.03	58.92	44	53.47	38.28	48.39	38.28	38.28	38.28
	Cmin 48 ≤ 2.5 mg/L (%)	92.99	80.49	92.07	78.04	87.77	75.5	87.77	75.5	83.68	71.44	79.72	71.44
150	Optimal dose (g)	3.6	> 5	3.75	> 5	3.9	> 5	4.05	> 5	4.2	> 5	4.35	> 5
	Target attainment (%)	92.01	86.63	92.01	85.36	92.01	83.57	92.01	83.57	92.01	83.57	92.01	83.57
	Cmin 24 ≤ 2.5 mg/L (%)	63.27	57.95	62.36	55.78	61.09	50.33	58.92	47.03	53.47	45.25	50.18	44
	Cmin 48 ≤ 2.5 mg/L (%)	92.99	87.77	92.99	87.77	92.99	86.13	92.07	82.17	87.77	79.72	87.77	79.72
160	Optimal dose (g)	3.65	> 5	3.8	> 5	3.95	> 5	4.1	> 5	4.25	> 5	4.4	> 5
	Target attainment (%)	92.01	80.55	92.01	80.55	92.01	80.55	92.01	80.55	92.01	80.55	92.01	80.55
	Cmin 24 ≤ 2.5 mg/L (%)	64.62	62.36	64.62	61.09	64.62	61.09	61.09	58.92	61.09	53.47	58.92	50.18
	Cmin 48 ≤ 2.5 mg/L (%)	92.99	92.99	92.99	92.07	92.99	87.77	92.99	87.77	92.07	87.77	92.07	87.77
170	Optimal dose (g)	3.65	> 5	3.8	> 5	3.95	> 5	4.1	> 5	4.25	> 5	4.4	> 5
	Target attainment (%)	92.01	80.55	92.01	80.55	92.01	80.55	92.01	80.55	92.01	80.55	92.01	80.55
	Cmin 24 ≤ 2.5 mg/L (%)	64.62	63.27	64.62	62.36	64.62	62.36	64.62	61.09	63.71	61.09	61.09	58.92
	Cmin 48 ≤ 2.5 mg/L (%)	92.99	92.99	92.99	92.99	92.99	92.99	92.99	92.07	92.99	92.07	92.07	92.07
180	Optimal dose (g)	3.7	> 5	3.85	> 5	4	> 5	4.15	> 5	4.3	> 5	4.45	> 5
	Target attainment (%)	92.01	80.55	92.01	80.55	92.01	80.55	92.01	80.55	92.01	80.55	92.01	80.55
	Cmin 24 ≤ 2.5 mg/L (%)	70.44	63.27	64.62	63.27	64.62	63.27	64.62	62.36	64.62	62.36	63.71	61.09

	Cmin 48 ≤ 2.5 mg/L (%)	92.99	92.99	92.99	92.99	92.99	92.99	92.99	92.99	92.99	92.99	92.07	
190	Optimal dose (g)	3.75	> 5	3.9	> 5	4.05	> 5	4.2	> 5	4.35	> 5	4.5	> 5
	Target attainment (%)	92.01	80.55	92.01	80.55	92.01	80.55	92.01	80.55	92.01	77.84	92.01	77.84
	Cmin 24 ≤ 2.5 mg/L (%)	70.44	64.62	70.44	64.62	64.62	64.62	64.62	64.62	64.62	64.62	64.62	63.71
	Cmin 48 ≤ 2.5 mg/L (%)	94.47	92.99	94.47	92.99	92.99	92.99	92.99	92.99	92.99	92.99	92.99	92.99
200	Optimal dose (g)	3.75	> 5	3.9	> 5	4.05	> 5	4.2	> 5	4.35	> 5	4.5	> 5
	Target attainment (%)	92.01	80.55	92.01	77.84	92.01	77.84	92.01	77.84	92.01	77.84	92.01	77.84
	Cmin 24 ≤ 2.5 mg/L (%)	70.44	70.44	70.44	64.62	70.44	64.62	70.44	64.62	64.62	64.62	64.62	64.62
	Cmin 48 ≤ 2.5 mg/L (%)	94.47	92.99	94.47	92.99	94.47	92.99	92.99	92.99	92.99	92.99	92.99	92.99
210	Optimal dose (g)	3.8	> 5	3.95	> 5	4.1	> 5	4.25	> 5	4.4	> 5	4.55	> 5
	Target attainment (%)	92.01	59.42	92.01	59.42	92.01	59.42	92.01	59.42	92.01	59.42	92.01	59.42
	Cmin 24 ≤ 2.5 mg/L (%)	77.08	70.44	70.44	70.44	70.44	70.44	70.44	64.62	70.44	64.62	64.62	64.62
	Cmin 48 ≤ 2.5 mg/L (%)	94.47	92.99	94.47	92.99	94.47	92.99	94.47	92.99	94.47	92.99	92.99	92.99
220	Optimal dose (g)	3.8	> 5	3.95	> 5	4.1	> 5	4.25	> 5	4.4	> 5	4.55	> 5
	Target attainment (%)	92.01	59.42	92.01	59.42	92.01	47.31	92.01	41.59	92.01	41.59	92.01	41.59
	Cmin 24 ≤ 2.5 mg/L (%)	78.44	70.44	77.08	70.44	74.41	70.44	70.44	70.44	70.44	70.44	70.44	64.62
	Cmin 48 ≤ 2.5 mg/L (%)	94.47	94.47	94.47	94.47	94.47	94.47	94.47	92.99	94.47	92.99	94.47	92.99
230	Optimal dose (g)	3.85	> 5	4	> 5	4.15	> 5	4.3	> 5	4.45	> 5	4.6	> 5
	Target attainment (%)	93.28	41.59	92.01	41.59	92.01	41.59	92.01	41.59	92.01	41.59	92.01	41.59
	Cmin 24 ≤ 2.5 mg/L (%)	78.44	71.44	78.44	70.44	77.08	70.44	74.41	70.44	70.44	70.44	70.44	70.44
	Cmin 48 ≤ 2.5 mg/L (%)	96.83	94.47	96.83	94.47	94.47	94.47	94.47	94.47	94.47	94.47	94.47	94.47
240	Optimal dose (g)	3.9	> 5	4.05	> 5	4.2	> 5	4.35	> 5	4.5	> 5	4.65	> 5
	Target attainment (%)	93.28	41.59	93.28	41.59	92.01	41.59	92.01	41.59	92.01	41.59	92.01	41.59
	Cmin 24 ≤ 2.5 mg/L (%)	78.44	78.44	78.44	77.08	78.44	74.41	77.08	70.44	74.41	70.44	70.44	70.44
	Cmin 48 ≤ 2.5 mg/L (%)	96.83	94.47	96.83	94.47	96.83	94.47	94.47	94.47	94.47	94.47	94.47	94.47
250	Optimal dose (g)	3.9	> 5	4.05	> 5	4.2	> 5	4.35	> 5	4.5	> 5	4.65	> 5
	Target attainment (%)	93.28	41.59	92.01	41.59	92.01	41.59	92.01	41.59	92.01	41.59	92.01	40.35

Cmin 24 ≤ 2.5 mg/L (%)	85.27	78.44	78.44	78.44	78.44	77.08	78.44	76.09	77.08	74.41	76.09	74.41
Cmin 48 ≤ 2.5 mg/L (%)	96.83	94.47	96.83	94.47	96.83	94.47	96.83	94.47	94.47	94.47	94.47	94.47

Table S2: Optimal initial amikacin dosing recommendations based on CLCG and BSA with associated efficacy and safety target attainment rates assuming a MIC value of 4 mg/L

Abbreviations: BSA, Body Surface Area; CLCG, Creatinine clearance estimated by Cockcroft & Gault equation; MIC, bacterial minimal inhibitory concentration; C_{max}/MIC ≥ 8, probability of amikacin maximal plasma concentration over MIC ratio ≥ 8, AUC/MIC ≥ 75, probability of amikacin daily area under the curve over MIC ratio ≥ 75; C_{min} 24 ≤ 2.5 mg/L, amikacin plasma concentration at 24h ≤ 2.5 mg/L probability; C_{min} 48, amikacin plasma concentration at 48h ≤ 2.5 mg/L probability.

The maximal dose was capped to 5 g.

	BSA (m ²)	1.5		1.6		1.7		1.8		1.9	
CLCG (mL/min)	Targeted index	C _{max} /MIC ≥ 8	AUC/MIC ≥ 75	C _{max} /MIC ≥ 8	AUC/MIC ≥ 75	C _{max} /MIC ≥ 8	AUC/MIC ≥ 75	C _{max} /MIC ≥ 8	AUC/MIC ≥ 75	C _{max} /MIC ≥ 8	AUC/MIC ≥ 75
10	Optimal dose (g)	1.2	0.75	1.3	0.8	1.35	0.85	1.45	0.85	1.5	0.9
	Target attainment (%)	92.01	90.27	92.01	92.39	92.01	94.56	92.01	92.39	92.01	92.39
	C _{min} 24 ≤ 2.5 mg/L (%)	0	1.81	0	0	0	0	0	0	0	0
	C _{min} 48 ≤ 2.5 mg/L (%)	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81
20	Optimal dose (g)	1.25	0.85	1.3	0.9	1.4	0.9	1.45	0.95	1.55	1
	Target attainment (%)	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27
	C _{min} 24 ≤ 2.5 mg/L (%)	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81
	C _{min} 48 ≤ 2.5 mg/L (%)	6.84	14.21	6.84	10.29	3.93	10.29	1.81	10.29	1.81	10.29
30	Optimal dose (g)	1.25	1	1.3	1	1.4	1.05	1.45	1.05	1.55	1.1
	Target attainment (%)	92.01	92.98	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27
	C _{min} 24 ≤ 2.5 mg/L (%)	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81
	C _{min} 48 ≤ 2.5 mg/L (%)	18.18	58.89	18.18	58.89	13.3	44.42	13.3	41.23	10.29	18.18
40	Optimal dose (g)	1.25	1.1	1.35	1.15	1.4	1.15	1.5	1.2	1.55	1.2
	Target attainment (%)	92.01	92.98	92.01	92.98	92.01	90.27	92.01	90.27	92.01	90.27
	C _{min} 24 ≤ 2.5 mg/L (%)	10.29	10.29	4.72	10.29	4.72	6.84	1.81	4.72	1.81	4.72
	C _{min} 48 ≤ 2.5 mg/L (%)	63.27	63.27	63.27	63.27	58.89	63.27	58.89	63.27	44.42	63.27

50	Optimal dose (g)	1.3	1.25	1.35	1.25	1.45	1.3	1.5	1.3	1.6	1.35
	Target attainment (%)	92.01	90.08	92.01	90.08	92.01	92.98	92.01	90.08	92.01	92.98
	Cmin 24 ≤ 2.5 mg/L (%)	10.29	10.29	10.29	10.29	10.29	10.29	10.29	10.29	4.72	10.29
	Cmin 48 ≤ 2.5 mg/L (%)	64.62	67.34	64.62	64.62	63.27	64.62	63.27	64.62	63.27	63.27
60	Optimal dose (g)	1.3	1.4	1.35	1.45	1.45	1.45	1.5	1.45	1.6	1.45
	Target attainment (%)	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08
	Cmin 24 ≤ 2.5 mg/L (%)	40.07	25.42	25.42	13.3	13.3	13.3	10.29	10.29	10.29	10.29
	Cmin 48 ≤ 2.5 mg/L (%)	74.15	74.15	74.15	74.15	74.15	74.15	70.44	71.44	64.62	70.44
70	Optimal dose (g)	1.3	1.6	1.4	1.6	1.45	1.6	1.55	1.6	1.6	1.65
	Target attainment (%)	92.01	92.25	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08
	Cmin 24 ≤ 2.5 mg/L (%)	63.27	45.79	50.33	40.07	40.07	38.28	38.28	28.61	28.61	28.61
	Cmin 48 ≤ 2.5 mg/L (%)	88.69	80.49	87.77	78.44	82.17	74.15	74.15	74.15	74.15	74.15
80	Optimal dose (g)	1.35	1.75	1.4	1.75	1.5	1.75	1.55	1.8	1.65	1.8
	Target attainment (%)	92.01	92.25	92.01	92.25	92.01	90.08	92.01	92.25	92.01	90.08
	Cmin 24 ≤ 2.5 mg/L (%)	63.27	57.95	63.27	57.95	62	45.79	53.47	40.07	45.79	38.28
	Cmin 48 ≤ 2.5 mg/L (%)	92.99	88.69	92.99	87.77	92.99	86.13	87.77	82.17	86.13	78.04
90	Optimal dose (g)	1.35	1.9	1.4	1.9	1.5	1.95	1.55	1.95	1.65	1.95
	Target attainment (%)	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	64.62	63.27	64.62	63.27	63.27	61.09	63.27	53.47	61.09	50.18
	Cmin 48 ≤ 2.5 mg/L (%)	92.99	92.99	92.99	92.99	92.99	87.77	92.99	87.77	92.99	87.77
100	Optimal dose (g)	1.35	2.05	1.45	2.1	1.5	2.1	1.6	2.1	1.65	2.1
	Target attainment (%)	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	70.44	63.27	64.62	63.27	64.62	63.27	64.62	62.36	64.62	61.09
	Cmin 48 ≤ 2.5 mg/L (%)	94.47	92.99	92.99	92.99	92.99	92.99	92.99	92.99	92.99	92.07
110	Optimal dose (g)	1.4	2.2	1.45	2.25	1.55	2.25	1.6	2.25	1.7	2.25
	Target attainment (%)	93.28	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	71.44	63.27	70.44	63.27	70.44	63.27	64.62	63.27	64.62	63.27

	Cmin 48 ≤ 2.5 mg/L (%)	94.47	92.99	94.47	92.99	94.47	92.99	92.99	92.99	92.99	92.99
120	Optimal dose (g)	1.4	2.4	1.45	2.4	1.55	2.4	1.6	2.4	1.7	2.4
	Target attainment (%)	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	78.44	64.62	75.4	64.62	70.44	64.62	70.44	64.62	64.62	63.27
	Cmin 48 ≤ 2.5 mg/L (%)	96.83	92.99	94.47	92.99	94.47	92.99	94.47	92.99	94.47	92.99
130	Optimal dose (g)	1.4	2.55	1.5	2.55	1.55	2.55	1.65	2.55	1.7	2.55
	Target attainment (%)	92.01	92.25	93.28	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	83.68	70.44	78.44	64.62	77.08	64.62	70.44	64.62	70.44	64.62
	Cmin 48 ≤ 2.5 mg/L (%)	96.83	92.99	96.83	92.99	96.83	92.99	94.47	92.99	94.47	92.99
140	Optimal dose (g)	1.4	2.7	1.5	2.7	1.55	2.7	1.65	2.7	1.75	2.7
	Target attainment (%)	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	92.07	70.44	83.68	70.44	78.44	70.44	77.08	64.62	74.41	64.62
	Cmin 48 ≤ 2.5 mg/L (%)	96.83	94.47	96.83	92.99	96.83	92.99	96.83	92.99	94.47	92.99
150	Optimal dose (g)	1.45	2.85	1.5	2.85	1.6	2.85	1.65	2.85	1.75	2.85
	Target attainment (%)	93.28	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	92.07	70.44	92.07	70.44	83.68	70.44	78.44	70.44	78.44	64.62
	Cmin 48 ≤ 2.5 mg/L (%)	96.83	94.47	96.83	94.47	96.83	94.47	96.83	92.99	96.83	92.99
160	Optimal dose (g)	1.45	2.95	1.55	3	1.6	3	1.7	3	1.75	3
	Target attainment (%)	93.28	92.25	93.28	92.25	92.01	92.25	93.28	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	92.07	71.44	92.07	70.44	90.55	70.44	83.68	70.44	78.44	70.44
	Cmin 48 ≤ 2.5 mg/L (%)	96.83	94.47	96.83	94.47	96.83	94.47	96.83	94.47	96.83	94.47
170	Optimal dose (g)	1.45	3.1	1.55	3.15	1.6	3.15	1.7	3.15	1.75	3.15
	Target attainment (%)	92.01	92.25	93.28	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	92.99	72.79	92.07	71.44	92.07	70.44	89.62	70.44	83.68	70.44
	Cmin 48 ≤ 2.5 mg/L (%)	99.28	94.47	96.83	94.47	96.83	94.47	96.83	94.47	96.83	94.47
180	Optimal dose (g)	1.5	3.25	1.55	3.25	1.65	3.3	1.7	3.3	1.8	3.3
	Target attainment (%)	93.28	92.25	93.28	92.25	93.28	92.25	92.01	92.25	93.28	92.25

	Cmin 24 ≤ 2.5 mg/L (%)	94.47	78.44	94.47	74.47	92.07	71.44	92.07	70.44	89.62	70.44
	Cmin 48 ≤ 2.5 mg/L (%)	100	94.47	99.28	94.47	96.83	94.47	96.83	94.47	96.83	94.47
190	Optimal dose (g)	1.5	3.4	1.6	3.4	1.65	3.4	1.75	3.45	1.8	3.45
	Target attainment (%)	91.47	92.25	93.28	92.25	93.28	92.25	93.28	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	94.47	80.97	94.47	78.44	94.47	78.44	92.07	77.08	92.07	70.44
	Cmin 48 ≤ 2.5 mg/L (%)	100	96.83	100	94.47	99.28	94.47	99.28	94.47	96.83	94.47
200	Optimal dose (g)	1.5	3.55	1.6	3.55	1.65	3.55	1.75	3.55	1.8	3.6
	Target attainment (%)	91.47	92.25	93.28	92.25	93.28	92.25	93.28	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	94.47	83.68	94.47	80.97	94.47	78.44	93.56	78.44	92.07	77.08
	Cmin 48 ≤ 2.5 mg/L (%)	100	96.83	100	96.83	100	94.47	99.28	94.47	99.28	94.47
210	Optimal dose (g)	1.55	3.7	1.6	3.7	1.7	3.7	1.75	3.7	1.85	3.7
	Target attainment (%)	91.47	92.25	91.47	92.25	93.28	92.25	93.28	92.25	93.28	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	94.47	85.32	94.47	83.68	94.47	78.44	94.47	78.44	93.56	78.44
	Cmin 48 ≤ 2.5 mg/L (%)	100	96.83	100	96.83	100	96.83	100	94.47	100	94.47
220	Optimal dose (g)	1.55	3.8	1.6	3.85	1.7	3.85	1.75	3.85	1.85	3.85
	Target attainment (%)	91.47	92.25	91.47	92.25	91.47	92.25	93.28	92.25	93.28	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	96.83	92.07	96.83	85.32	94.47	80.97	94.47	78.44	94.47	78.44
	Cmin 48 ≤ 2.5 mg/L (%)	100	96.83	100	96.83	100	96.83	100	96.83	100	96.83
230	Optimal dose (g)	1.55	3.95	1.65	3.95	1.7	4	1.8	4	1.85	4
	Target attainment (%)	91.47	92.25	91.47	92.25	91.47	92.25	93.28	92.25	93.28	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	96.83	92.07	96.83	92.07	96.83	85.32	94.47	80.97	94.47	78.44
	Cmin 48 ≤ 2.5 mg/L (%)	100	96.83	100	96.83	100	96.83	100	96.83	100	96.83
240	Optimal dose (g)	1.6	4.1	1.65	4.1	1.75	4.1	1.8	4.1	1.9	4.15
	Target attainment (%)	92.39	92.25	91.47	92.25	91.47	92.25	91.47	92.25	93.28	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	96.83	92.07	96.83	92.07	96.83	92.07	96.83	83.68	94.47	80.97
	Cmin 48 ≤ 2.5 mg/L (%)	100	96.83	100	96.83	100	96.83	100	96.83	100	96.83
250	Optimal dose (g)	1.6	4.2	1.65	4.25	1.75	4.25	1.8	4.25	1.9	4.25

Target attainment (%)	92.39	92.25	91.47	92.25	91.47	92.25	91.47	92.25	91.47	92.25
Cmin 24 ≤ 2.5 mg/L (%)	96.83	92.07	96.83	92.07	96.83	92.07	96.83	89.62	96.83	80.97
Cmin 48 ≤ 2.5 mg/L (%)	100	96.83	100	96.83	100	96.83	100	96.83	100	96.83

Table

Table S2 continued

CLCG (mL/min)	BSA (m2) Targeted index	2		2.1		2.2		2.3		2.4		2.5	
		Cmax/MIC ≥ 8	AUC/MIC ≥ 75	Cmax/MIC ≥ 8	AUC/MIC ≥ 75	Cmax/MIC ≥ 8	AUC/MIC ≥ 75	Cmax/MIC ≥ 8	AUC/MIC ≥ 75	Cmax/MIC ≥ 8	AUC/MIC ≥ 75	Cmax/MIC ≥ 8	AUC/MIC ≥ 75
10	Optimal dose (g)	1.6	0.9	1.65	0.95	1.75	1	1.8	1	1.9	1.05	1.95	1.05
	Target attainment (%)	92.01	91.47	92.01	93.28	92.01	94.2	92.01	93.28	92.01	93.28	92.01	93.28
	Cmin 24 ≤ 2.5 mg/L (%)	0	0	0	0	0	0	0	0	0	0	0	0
	Cmin 48 ≤ 2.5 mg/L (%)	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	0	1.81	0	1.81
20	Optimal dose (g)	1.6	1	1.7	1.05	1.75	1.1	1.85	1.1	1.9	1.15	2	1.2
	Target attainment (%)	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27
	Cmin 24 ≤ 2.5 mg/L (%)	1.81	1.81	1.81	1.81	1.81	1.81	0	1.81	0	1.81	0	1.81
	Cmin 48 ≤ 2.5 mg/L (%)	1.81	10.29	1.81	6.84	1.81	6.84	1.81	6.84	1.81	1.81	1.81	1.81
30	Optimal dose (g)	1.65	1.15	1.7	1.15	1.8	1.2	1.85	1.2	1.95	1.25	2	1.3
	Target attainment (%)	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27
	Cmin 24 ≤ 2.5 mg/L (%)	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81
	Cmin 48 ≤ 2.5 mg/L (%)	10.29	16	10.29	16	10.29	13.3	10.29	13.3	6.84	10.29	6.84	10.29
40	Optimal dose (g)	1.65	1.25	1.7	1.25	1.8	1.3	1.85	1.35	1.95	1.35	2.05	1.4
	Target attainment (%)	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27

	Cmin 24 ≤ 2.5 mg/L (%)	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	
	Cmin 48 ≤ 2.5 mg/L (%)	39.96	60.13	17.27	60.13	13.3	58.89	13.3	53.44	13.3	48.87	10.29	43.15
50	Optimal dose (g)	1.65	1.35	1.75	1.4	1.8	1.4	1.9	1.45	1.95	1.45	2.05	1.5
	Target attainment (%)	92.01	90.27	92.01	92.98	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27
	Cmin 24 ≤ 2.5 mg/L (%)	4.72	10.29	1.81	4.72	1.81	4.72	1.81	4.72	1.81	1.81	1.81	1.81
	Cmin 48 ≤ 2.5 mg/L (%)	63.27	63.27	60.13	63.27	60.13	63.27	58.89	63.27	52.16	63.27	42.24	63.27
60	Optimal dose (g)	1.7	1.5	1.75	1.5	1.85	1.55	1.9	1.55	2	1.6	2.05	1.6
	Target attainment (%)	92.01	90.08	92.01	90.08	92.01	92.98	92.01	90.27	92.01	92.98	92.01	90.27
	Cmin 24 ≤ 2.5 mg/L (%)	10.29	10.29	10.29	10.29	4.72	10.29	4.72	10.29	4.72	6.84	1.81	4.72
	Cmin 48 ≤ 2.5 mg/L (%)	64.62	70.44	63.27	64.62	63.27	64.62	63.27	64.62	63.27	64.62	63.27	63.27
70	Optimal dose (g)	1.7	1.65	1.75	1.65	1.85	1.65	1.9	1.65	2	1.7	2.05	1.75
	Target attainment (%)	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08	92.01	92.98
	Cmin 24 ≤ 2.5 mg/L (%)	10.29	16.5	10.29	10.29	10.29	10.29	10.29	10.29	10.29	10.29	6.84	10.29
	Cmin 48 ≤ 2.5 mg/L (%)	71.44	74.15	70.44	71.44	70.44	71.44	64.62	70.44	64.62	70.44	64.62	70.44
80	Optimal dose (g)	1.7	1.8	1.8	1.8	1.85	1.8	1.95	1.8	2	1.85	2.1	1.85
	Target attainment (%)	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08
	Cmin 24 ≤ 2.5 mg/L (%)	38.28	38.28	28.61	28.61	28.61	28.61	13.48	25.59	13.48	13.48	10.29	13.48
	Cmin 48 ≤ 2.5 mg/L (%)	83.68	75.5	75.5	75.5	74.15	74.15	71.44	71.44	70.44	71.44	70.44	71.44
90	Optimal dose (g)	1.7	1.95	1.8	1.95	1.9	1.95	1.95	2	2.05	2	2.1	2
	Target attainment (%)	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08
	Cmin 24 ≤ 2.5 mg/L (%)	53.47	45.79	50.18	38.28	38.28	38.28	38.28	38.28	28.61	28.61	25.59	28.61
	Cmin 48 ≤ 2.5 mg/L (%)	92.07	86.13	87.77	86.13	83.68	83.68	81.15	77.19	75.5	77.19	71.44	71.44
100	Optimal dose (g)	1.75	2.1	1.8	2.1	1.9	2.1	1.95	2.15	2.05	2.15	2.1	2.15

	Target attainment (%)	92.01	92.25	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08
	Cmin 24 ≤ 2.5 mg/L (%)	63.27	58.92	61.09	50.18	53.47	50.18	50.18	41.42	41.42	41.42	41.42	41.42
	Cmin 48 ≤ 2.5 mg/L (%)	92.99	92.07	92.99	87.77	92.07	87.77	92.07	86.13	86.13	83.68	83.68	83.68
110	Optimal dose (g)	1.75	2.25	1.85	2.25	1.9	2.3	2	2.3	2.05	2.3	2.15	2.3
	Target attainment (%)	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	90.08	92.01	90.08
	Cmin 24 ≤ 2.5 mg/L (%)	64.62	61.09	64.62	61.09	63.35	53.47	61.09	50.18	53.47	50.18	50.18	47.14
	Cmin 48 ≤ 2.5 mg/L (%)	92.99	92.99	92.99	92.07	92.99	92.07	92.99	92.07	92.07	87.77	92.07	87.77
120	Optimal dose (g)	1.75	2.4	1.85	2.4	1.9	2.45	2	2.45	2.05	2.45	2.15	2.45
	Target attainment (%)	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	90.08
	Cmin 24 ≤ 2.5 mg/L (%)	64.62	63.27	64.62	62.36	64.62	61.09	64.62	58.92	63.35	53.47	60.27	50.18
	Cmin 48 ≤ 2.5 mg/L (%)	94.47	92.99	92.99	92.99	92.99	92.99	92.99	92.07	92.99	92.07	92.07	92.07
130	Optimal dose (g)	1.8	2.55	1.85	2.6	1.95	2.6	2	2.6	2.1	2.6	2.15	2.6
	Target attainment (%)	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	70.44	64.62	64.62	64.62	64.62	64.62	64.62	62.44	64.62	62.44	64.62	58.92
	Cmin 48 ≤ 2.5 mg/L (%)	94.47	92.99	94.47	92.99	94.47	92.99	92.99	92.99	92.99	92.07	92.99	92.07
140	Optimal dose (g)	1.8	2.7	1.9	2.75	1.95	2.75	2.05	2.75	2.1	2.75	2.2	2.75
	Target attainment (%)	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	70.44	64.62	70.44	64.62	64.62	64.62	64.62	64.62	64.62	62.44	64.62	62.44
	Cmin 48 ≤ 2.5 mg/L (%)	94.47	92.99	94.47	92.99	94.47	92.99	94.47	92.99	94.47	92.99	92.99	92.99
150	Optimal dose (g)	1.8	2.85	1.9	2.9	1.95	2.9	2.05	2.9	2.1	2.9	2.2	2.9
	Target attainment (%)	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	77.08	64.62	70.44	64.62	70.44	64.62	70.44	64.62	64.62	64.62	64.62	63.71
	Cmin 48 ≤ 2.5 mg/L (%)	96.83	92.99	94.47	92.99	94.47	92.99	94.47	92.99	94.47	92.99	94.47	92.99

160	Optimal dose (g)	1.85	3	1.9	3	2	3.05	2.05	3.05	2.15	3.05	2.2	3.05
	Target attainment (%)	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	78.44	70.44	77.08	64.62	74.41	64.62	70.44	64.62	70.44	64.62	64.62	64.62
	Cmin 48 ≤ 2.5 mg/L (%)	96.83	92.99	96.83	92.99	96.83	92.99	94.47	92.99	94.47	92.99	94.47	92.99
170	Optimal dose (g)	1.85	3.15	1.9	3.15	2	3.2	2.05	3.2	2.15	3.2	2.2	3.2
	Target attainment (%)	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	78.44	70.44	78.44	70.44	77.08	64.62	76.09	64.62	74.41	64.62	70.44	64.62
	Cmin 48 ≤ 2.5 mg/L (%)	96.83	94.47	96.83	94.47	96.83	92.99	96.83	92.99	96.83	92.99	96.83	92.99
180	Optimal dose (g)	1.85	3.3	1.95	3.3	2	3.3	2.1	3.35	2.15	3.35	2.25	3.35
	Target attainment (%)	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	83.68	70.44	78.44	70.44	78.44	70.44	77.08	64.62	76.09	64.62	74.41	64.62
	Cmin 48 ≤ 2.5 mg/L (%)	96.83	94.47	96.83	94.47	96.83	94.47	96.83	94.47	96.83	94.47	96.83	94.47
190	Optimal dose (g)	1.9	3.45	1.95	3.45	2.05	3.45	2.1	3.45	2.2	3.5	2.25	3.5
	Target attainment (%)	93.28	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	89.62	70.44	83.68	70.44	78.44	70.44	78.44	70.44	77.08	64.62	76.09	64.62
	Cmin 48 ≤ 2.5 mg/L (%)	96.83	94.47	96.83	94.47	96.83	94.47	96.83	94.47	96.83	94.47	96.83	94.47
200	Optimal dose (g)	1.9	3.6	1.95	3.6	2.05	3.6	2.1	3.6	2.2	3.6	2.25	3.65
	Target attainment (%)	93.28	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	92.07	74.41	89.62	70.44	80.97	70.44	78.44	70.44	78.44	70.44	78.44	70.44
	Cmin 48 ≤ 2.5 mg/L (%)	96.83	94.47	96.83	94.47	96.83	94.47	96.83	94.47	96.83	94.47	96.83	94.47
210	Optimal dose (g)	1.9	3.75	2	3.75	2.05	3.75	2.15	3.75	2.2	3.75	2.3	3.75
	Target attainment (%)	92.01	92.25	93.28	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	92.07	77.08	92.07	76.09	89.62	74.41	80.97	70.44	78.44	70.44	78.44	70.44

	Cmin 48 ≤ 2.5 mg/L (%)	99.28	94.47	96.83	94.47	96.83	94.47	96.83	94.47	96.83	94.47	96.83	94.47
220	Optimal dose (g)	1.9	3.85	2	3.9	2.05	3.9	2.15	3.9	2.2	3.9	2.3	3.9
	Target attainment (%)	92.01	92.25	93.28	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	93.56	78.44	93.56	77.08	92.07	76.09	89.62	74.41	80.97	74.41	78.44	70.44
	Cmin 48 ≤ 2.5 mg/L (%)	100	94.47	99.28	94.47	99.28	94.47	96.83	94.47	96.83	94.47	96.83	94.47
230	Optimal dose (g)	1.95	4	2	4	2.1	4.05	2.15	4.05	2.25	4.05	2.3	4.05
	Target attainment (%)	93.28	92.25	92.01	92.25	93.28	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	93.56	78.44	93.56	78.44	93.56	77.08	92.07	76.09	87.99	74.41	80.97	74.41
	Cmin 48 ≤ 2.5 mg/L (%)	100	96.83	100	96.83	99.28	94.47	99.28	94.47	96.83	94.47	96.83	94.47
240	Optimal dose (g)	1.95	4.15	2.05	4.15	2.1	4.15	2.2	4.15	2.25	4.2	2.35	4.2
	Target attainment (%)	93.28	92.25	93.28	92.25	92.01	92.25	93.28	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	94.47	78.44	93.56	78.44	93.56	78.44	93.56	77.08	89.62	76.09	87.99	74.41
	Cmin 48 ≤ 2.5 mg/L (%)	100	96.83	100	96.83	100	96.83	100	96.83	99.28	94.47	96.83	94.47
250	Optimal dose (g)	1.95	4.3	2.05	4.3	2.1	4.3	2.2	4.3	2.25	4.3	2.35	4.3
	Target attainment (%)	93.28	92.25	93.28	92.25	92.01	92.25	93.28	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	94.47	80.97	94.47	78.44	93.56	78.44	93.56	78.44	93.56	77.08	89.62	76.09
	Cmin 48 ≤ 2.5 mg/L (%)	100	96.83	100	96.83	100	96.83	100	96.83	100	96.83	99.28	96.83

Table S3: Optimal initial amikacin dosing recommendations based on CLCG and BSA with associated efficacy and safety target attainment rates assuming a MIC value of 2 mg/L

Abbreviations: BSA, Body Surface Area; CLCG, Creatinine clearance estimated by Cockcroft & Gault equation; MIC, bacterial minimal inhibitory concentration; C_{max}/MIC ≥ 8, probability of amikacin maximal plasma concentration over MIC ratio ≥ 8, AUC/MIC ≥ 75, probability of amikacin daily area under the curve over MIC ratio ≥ 75; C_{min} 24 ≤ 2.5 mg/L, amikacin plasma concentration at 24h ≤ 2.5 mg/L probability; C_{min} 48, amikacin plasma concentration at 48h ≤ 2.5 mg/L probability.

The maximal dose was capped to 5 g.

	BSA (m ²)	1.5		1.6		1.7		1.8		1.9	
CLCG(mL/min)	Targeted index	C _{max} /MIC ≥ 8	AUC/MIC ≥ 75	C _{max} /MIC ≥ 8	AUC/MIC ≥ 75	C _{max} /MIC ≥ 8	AUC/MIC ≥ 75	C _{max} /MIC ≥ 8	AUC/MIC ≥ 75	C _{max} /MIC ≥ 8	AUC/MIC ≥ 75
10	Optimal dose (g)	0.6	0.5	0.65	0.5	0.7	0.5	0.75	0.5	0.75	0.5
	Target attainment (%)	92.01	99.09	92.01	99.09	92.01	99.09	92.01	99.09	92.01	96.38
	C _{min} 24 ≤ 2.5 mg/L (%)	1.81	1.81	1.81	1.81	0	1.81	0	1.81	0	1.81
	C _{min} 48 ≤ 2.5 mg/L (%)	3.93	6.84	1.81	6.84	1.81	6.84	1.81	7.75	1.81	4.84
20	Optimal dose (g)	0.65	0.5	0.65	0.5	0.7	0.5	0.75	0.5	0.8	0.5
	Target attainment (%)	92.01	97.28	92.01	97.28	92.01	92.44	92.01	90.27	92.01	90.27
	C _{min} 24 ≤ 2.5 mg/L (%)	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81
	C _{min} 48 ≤ 2.5 mg/L (%)	19.45	58.89	19.45	58.89	18.18	58.89	14.21	58.89	11.2	58.89
30	Optimal dose (g)	0.65	0.5	0.65	0.5	0.7	0.55	0.75	0.55	0.8	0.55
	Target attainment (%)	92.01	92.98	92.01	90.27	92.01	92.98	92.01	90.27	92.01	90.27
	C _{min} 24 ≤ 2.5 mg/L (%)	10.29	14.21	10.29	14.21	6.84	10.29	4.72	10.29	1.81	10.29
	C _{min} 48 ≤ 2.5 mg/L (%)	65.99	77.52	65.99	77.52	63.27	74.15	63.27	74.15	60.13	73.16
40	Optimal dose (g)	0.65	0.55	0.7	0.6	0.7	0.6	0.75	0.6	0.8	0.6
	Target attainment (%)	92.01	92.98	92.01	92.98	92.01	92.98	92.01	90.27	92.01	90.27
	C _{min} 24 ≤ 2.5 mg/L (%)	40.98	53.44	13.3	43.15	13.3	40.98	10.29	29.52	10.29	29.52
	C _{min} 48 ≤ 2.5 mg/L (%)	81.41	92.99	76.6	88.69	74.15	84.72	74.15	84.72	73.16	83.09

50	Optimal dose (g)	0.65	0.65	0.7	0.65	0.75	0.65	0.75	0.65	0.8	0.7
	Target attainment (%)	92.01	92.98	92.01	92.98	92.01	92.98	92.01	90.08	92.01	92.98
	Cmin 24 ≤ 2.5 mg/L (%)	63.27	63.27	63.27	63.27	48.87	63.27	40.98	63.27	28.61	43.15
	Cmin 48 ≤ 2.5 mg/L (%)	92.99	92.99	92.99	92.99	88.69	92.99	88.69	92.99	86.13	92.99
60	Optimal dose (g)	0.65	0.7	0.7	0.75	0.75	0.75	0.75	0.75	0.8	0.75
	Target attainment (%)	92.01	90.08	92.01	95.16	92.01	95.16	92.01	92.98	92.01	92.98
	Cmin 24 ≤ 2.5 mg/L (%)	64.62	64.62	64.62	63.27	63.27	63.27	63.27	63.27	63.27	63.27
	Cmin 48 ≤ 2.5 mg/L (%)	92.99	92.99	92.99	92.99	92.99	92.99	92.99	92.99	92.99	92.99
70	Optimal dose (g)	0.65	0.8	0.7	0.8	0.75	0.8	0.8	0.8	0.8	0.85
	Target attainment (%)	92.01	92.25	92.01	90.08	92.01	90.08	92.01	90.08	92.01	95.16
	Cmin 24 ≤ 2.5 mg/L (%)	70.44	64.62	70.44	64.62	64.62	64.62	64.62	64.62	64.62	64.62
	Cmin 48 ≤ 2.5 mg/L (%)	94.47	94.47	94.47	92.99	94.47	92.99	92.99	92.99	92.99	92.99
80	Optimal dose (g)	0.7	0.9	0.7	0.9	0.75	0.9	0.8	0.9	0.85	0.9
	Target attainment (%)	93.28	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	90.08
	Cmin 24 ≤ 2.5 mg/L (%)	79.8	70.44	75.4	70.44	70.44	64.62	70.44	64.62	64.62	64.62
	Cmin 48 ≤ 2.5 mg/L (%)	96.83	94.47	96.83	94.47	94.47	94.47	94.47	94.47	94.47	94.47
90	Optimal dose (g)	0.7	0.95	0.7	0.95	0.75	1	0.8	1	0.85	1
	Target attainment (%)	93.28	92.25	92.01	92.25	92.01	95.16	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	83.68	71.44	83.68	70.44	81.15	70.44	70.44	70.44	70.44	64.62
	Cmin 48 ≤ 2.5 mg/L (%)	96.83	94.47	96.83	94.47	96.83	94.47	96.83	94.47	94.47	94.47
100	Optimal dose (g)	0.7	1.05	0.75	1.05	0.75	1.05	0.8	1.05	0.85	1.05
	Target attainment (%)	93.28	92.25	93.28	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	92.07	77.08	87.77	71.44	83.68	70.44	81.15	70.44	77.08	70.44
	Cmin 48 ≤ 2.5 mg/L (%)	96.83	96.83	96.83	96.83	96.83	94.47	96.83	94.47	96.83	94.47
110	Optimal dose (g)	0.7	1.1	0.75	1.15	0.8	1.15	0.8	1.15	0.85	1.15
	Target attainment (%)	93.28	92.25	93.28	92.25	93.28	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	92.99	81.15	92.07	77.7	92.07	77.08	83.68	74.41	81.15	70.44

	Cmin 48 ≤ 2.5 mg/L (%)	100	96.83	99.28	96.83	96.83	96.83	96.83	96.83	96.83	96.83
120	Optimal dose (g)	0.7	1.2	0.75	1.2	0.8	1.2	0.8	1.2	0.85	1.2
	Target attainment (%)	92.01	92.25	93.28	92.25	93.28	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	94.47	83.68	94.47	81.15	92.07	78.44	92.07	77.7	92.07	77.08
	Cmin 48 ≤ 2.5 mg/L (%)	100	96.83	100	96.83	99.28	96.83	99.28	96.83	96.83	96.83
130	Optimal dose (g)	0.7	1.3	0.75	1.3	0.8	1.3	0.85	1.3	0.85	1.3
	Target attainment (%)	92.01	92.25	93.28	92.25	93.28	92.25	93.28	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	94.47	85.32	94.47	83.68	94.47	78.44	92.07	78.44	92.07	78.44
	Cmin 48 ≤ 2.5 mg/L (%)	100	96.83	100	96.83	100	96.83	100	96.83	100	96.83
140	Optimal dose (g)	0.7	1.35	0.75	1.35	0.8	1.35	0.85	1.35	0.9	1.35
	Target attainment (%)	92.01	92.25	92.01	92.25	93.28	92.25	93.28	92.25	93.28	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	96.83	92.07	94.47	89.62	94.47	83.68	94.47	81.15	94.47	78.44
	Cmin 48 ≤ 2.5 mg/L (%)	100	96.83	100	96.83	100	96.83	100	96.83	100	96.83
150	Optimal dose (g)	0.75	1.45	0.75	1.45	0.8	1.45	0.85	1.45	0.9	1.45
	Target attainment (%)	93.28	92.25	92.01	92.25	92.01	92.25	93.28	92.25	93.28	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	96.83	92.07	96.83	92.07	94.47	89.62	94.47	83.68	94.47	81.15
	Cmin 48 ≤ 2.5 mg/L (%)	100	96.83	100	96.83	100	96.83	100	96.83	100	96.83
160	Optimal dose (g)	0.75	1.5	0.8	1.5	0.8	1.5	0.85	1.5	0.9	1.5
	Target attainment (%)	93.28	92.25	93.28	92.25	92.01	92.25	93.28	92.25	93.28	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	96.83	92.07	96.83	92.07	96.83	92.07	96.83	89.62	94.47	83.68
	Cmin 48 ≤ 2.5 mg/L (%)	100	96.83	100	96.83	100	96.83	100	96.83	100	96.83
170	Optimal dose (g)	0.75	1.55	0.8	1.6	0.8	1.6	0.85	1.6	0.9	1.6
	Target attainment (%)	93.28	92.25	93.28	92.25	92.01	92.25	92.01	92.25	93.28	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	96.83	92.99	96.83	92.07	96.83	92.07	96.83	92.07	96.83	89.62
	Cmin 48 ≤ 2.5 mg/L (%)	100	99.28	100	96.83	100	96.83	100	96.83	100	96.83
180	Optimal dose (g)	0.75	1.65	0.8	1.65	0.85	1.65	0.85	1.65	0.9	1.65
	Target attainment (%)	93.28	92.25	93.28	92.25	93.28	92.25	92.01	92.25	93.28	92.25

	Cmin 24 ≤ 2.5 mg/L (%)	96.83	92.99	96.83	92.07	96.83	92.07	96.83	92.07	96.83	92.07
	Cmin 48 ≤ 2.5 mg/L (%)	100	99.28	100	99.28	100	96.83	100	96.83	100	96.83
190	Optimal dose (g)	0.75	1.7	0.8	1.7	0.85	1.7	0.9	1.75	0.9	1.75
	Target attainment (%)	91.47	92.25	93.28	92.25	93.28	92.25	93.28	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	96.83	94.47	96.83	94.47	96.83	92.07	96.83	92.07	96.83	92.07
	Cmin 48 ≤ 2.5 mg/L (%)	100	100	100	99.28	100	99.28	100	99.28	100	96.83
200	Optimal dose (g)	0.75	1.8	0.8	1.8	0.85	1.8	0.9	1.8	0.9	1.8
	Target attainment (%)	91.47	92.25	93.28	92.25	93.28	92.25	93.28	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	96.83	94.47	96.83	94.47	96.83	94.47	96.83	93.56	96.83	92.07
	Cmin 48 ≤ 2.5 mg/L (%)	100	100	100	100	100	99.28	100	99.28	100	99.28
210	Optimal dose (g)	0.8	1.85	0.8	1.85	0.85	1.85	0.9	1.85	0.95	1.85
	Target attainment (%)	92.39	92.25	91.47	92.25	93.28	92.25	93.28	92.25	93.28	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	96.83	94.47	96.83	94.47	96.83	94.47	96.83	94.47	96.83	93.56
	Cmin 48 ≤ 2.5 mg/L (%)	100	100	100	100	100	100	100	100	100	100
220	Optimal dose (g)	0.8	1.9	0.8	1.95	0.85	1.95	0.9	1.95	0.95	1.95
	Target attainment (%)	92.39	92.25	91.47	92.25	91.47	92.25	93.28	92.25	93.28	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	100	94.47	96.83	94.47	96.83	94.47	96.83	94.47	96.83	93.56
	Cmin 48 ≤ 2.5 mg/L (%)	100	100	100	100	100	100	100	100	100	100
230	Optimal dose (g)	0.8	2	0.85	2	0.85	2	0.9	2	0.95	2
	Target attainment (%)	92.39	92.25	92.39	92.25	91.47	92.25	93.28	92.25	93.28	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	100	94.47	97.55	94.47	96.83	94.47	96.83	94.47	96.83	94.47
	Cmin 48 ≤ 2.5 mg/L (%)	100	100	100	100	100	100	100	100	100	100
240	Optimal dose (g)	0.8	2.05	0.85	2.05	0.9	2.05	0.9	2.05	0.95	2.1
	Target attainment (%)	92.39	92.25	92.39	92.25	92.39	92.25	91.47	92.25	93.28	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	100	94.47	100	94.47	96.83	94.47	96.83	94.47	96.83	94.47
	Cmin 48 ≤ 2.5 mg/L (%)	100	100	100	100	100	100	100	100	100	100
250	Optimal dose (g)	0.8	2.1	0.85	2.15	0.9	2.15	0.9	2.15	0.95	2.15

Target attainment (%)	92.39	92.25	92.39	92.25	92.39	92.25	91.47	92.25	91.47	92.25
Cmin 24 ≤ 2.5 mg/L (%)	100	94.47	100	94.47	100	94.47	97.55	94.47	96.83	94.47
Cmin 48 ≤ 2.5 mg/L (%)	100	100	100	100	100	100	100	100	100	100

Table S3 continued

CLCG(mL/min)	BSA (m2)	2		2.1		2.2		2.3		2.4		2.5	
		Cmax/MIC ≥ 8	AUC/MIC ≥ 75	Cmax/MIC ≥ 8	AUC/MIC ≥ 75	Cmax/MIC ≥ 8	AUC/MIC ≥ 75	Cmax/MIC ≥ 8	AUC/MIC ≥ 75	Cmax/MIC ≥ 8	AUC/MIC ≥ 75	Cmax/MIC ≥ 8	AUC/MIC ≥ 75
10	Optimal dose (g)	0.8	0.5	0.85	0.5	0.9	0.5	0.9	0.5	0.95	0.55	1	0.55
	Target attainment (%)	92.01	96.38	92.01	96.38	92.01	94.2	92.01	93.28	92.01	96.38	92.01	93.28
	Cmin 24 ≤ 2.5 mg/L (%)	0	1.81	0	1.81	0	1.81	0	1.81	0	0	0	0
	Cmin 48 ≤ 2.5 mg/L (%)	1.81	4.84	1.81	4.84	1.81	4.84	1.81	4.84	1.81	1.81	1.81	2.72
20	Optimal dose (g)	0.8	0.5	0.85	0.55	0.9	0.55	0.95	0.55	0.95	0.6	1	0.6
	Target attainment (%)	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27
	Cmin 24 ≤ 2.5 mg/L (%)	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81	1.81
	Cmin 48 ≤ 2.5 mg/L (%)	10.29	58.89	10.29	49.98	10.29	41.23	10.29	41.23	10.29	19.45	6.84	19.45
30	Optimal dose (g)	0.85	0.6	0.85	0.6	0.9	0.6	0.95	0.6	1	0.65	1	0.65
	Target attainment (%)	92.01	92.44	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27
	Cmin 24 ≤ 2.5 mg/L (%)	1.81	6.84	1.81	6.84	1.81	6.84	1.81	6.84	1.81	1.81	1.81	1.81
	Cmin 48 ≤ 2.5 mg/L (%)	58.89	65.99	58.89	65.99	53.44	65.99	39.96	65.99	18.18	63.27	16	63.27
40	Optimal dose (g)	0.85	0.65	0.85	0.65	0.9	0.65	0.95	0.7	1	0.7	1.05	0.7
	Target attainment (%)	92.01	92.98	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27	92.01	90.27
	Cmin 24 ≤ 2.5 mg/L (%)	10.29	10.29	10.29	10.29	6.84	10.29	4.72	10.29	1.81	10.29	1.81	10.29

	Cmin 48 ≤ 2.5 mg/L (%)	64.62	74.15	64.62	74.15	63.27	74.15	63.27	74.15	63.27	73.16	63.27	73.16
50	Optimal dose (g)	0.85	0.7	0.9	0.7	0.9	0.7	0.95	0.75	1	0.75	1.05	0.75
	Target attainment (%)	92.01	92.98	92.01	92.98	92.01	90.27	92.01	92.98	92.01	90.27	92.01	90.27
	Cmin 24 ≤ 2.5 mg/L (%)	16.5	40.98	10.29	40.98	10.29	29.52	10.29	17.41	10.29	17.41	10.29	14.39
	Cmin 48 ≤ 2.5 mg/L (%)	75.5	92.99	74.15	88.69	74.15	88.69	73.16	86.13	70.44	86.13	64.62	86.13
60	Optimal dose (g)	0.85	0.75	0.9	0.75	0.95	0.8	0.95	0.8	1	0.8	1.05	0.8
	Target attainment (%)	92.01	90.08	92.01	90.08	92.01	92.98	92.01	92.98	92.01	92.98	92.01	90.27
	Cmin 24 ≤ 2.5 mg/L (%)	53.26	63.27	44.12	63.27	28.61	52.01	28.61	46.29	13.48	44.12	13.48	42.33
	Cmin 48 ≤ 2.5 mg/L (%)	92.99	92.99	88.69	92.99	86.13	92.99	86.13	92.99	81.15	92.99	74.15	92.99
70	Optimal dose (g)	0.85	0.85	0.9	0.85	0.95	0.85	0.95	0.85	1	0.85	1.05	0.9
	Target attainment (%)	92.01	92.98	92.01	92.98	92.01	92.98	92.01	92.98	92.01	90.08	92.01	92.98
	Cmin 24 ≤ 2.5 mg/L (%)	64.62	64.62	63.27	64.62	56.55	63.27	53.26	63.27	44.12	63.27	41.42	53.26
	Cmin 48 ≤ 2.5 mg/L (%)	92.99	92.99	92.99	92.99	92.99	92.99	92.99	92.99	92.99	92.99	87.77	92.99
80	Optimal dose (g)	0.85	0.9	0.9	0.9	0.95	0.9	1	0.9	1	0.95	1.05	0.95
	Target attainment (%)	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08	92.01	92.98	92.01	92.98
	Cmin 24 ≤ 2.5 mg/L (%)	64.62	64.62	64.62	64.62	64.62	64.62	64.62	64.62	64.62	64.62	56.55	64.62
	Cmin 48 ≤ 2.5 mg/L (%)	94.47	94.47	92.99	92.99	92.99	92.99	92.99	92.99	92.99	92.99	92.99	92.99
90	Optimal dose (g)	0.85	1	0.9	1	0.95	1	1	1	1.05	1	1.05	1
	Target attainment (%)	92.01	92.25	92.01	92.25	92.01	90.08	92.01	90.08	92.01	90.08	92.01	90.08
	Cmin 24 ≤ 2.5 mg/L (%)	70.44	64.62	64.62	64.62	64.62	64.62	64.62	64.62	64.62	64.62	64.62	64.62
	Cmin 48 ≤ 2.5 mg/L (%)	94.47	94.47	94.47	94.47	94.47	94.47	94.47	94.47	92.99	94.47	92.99	94.47
100	Optimal dose (g)	0.9	1.05	0.9	1.05	0.95	1.05	1	1.1	1.05	1.1	1.05	1.1
	Target attainment (%)	92.01	92.25	92.01	90.08	92.01	90.08	92.01	92.25	92.01	92.25	92.01	90.08

	Cmin 24 ≤ 2.5 mg/L (%)	70.44	70.44	70.44	64.62	70.44	64.62	64.62	64.62	64.62	64.62	64.62	64.62
	Cmin 48 ≤ 2.5 mg/L (%)	96.83	94.47	96.83	94.47	94.47	94.47	94.47	94.47	94.47	94.47	94.47	94.47
110	Optimal dose (g)	0.9	1.15	0.95	1.15	0.95	1.15	1	1.15	1.05	1.15	1.1	1.15
	Target attainment (%)	92.01	92.25	93.28	92.25	92.01	92.25	92.01	92.25	92.01	90.08	92.01	90.08
	Cmin 24 ≤ 2.5 mg/L (%)	78.44	70.44	74.41	70.44	74.41	70.44	70.44	64.62	70.44	64.62	64.62	64.62
	Cmin 48 ≤ 2.5 mg/L (%)	96.83	94.47	96.83	94.47	96.83	94.47	96.83	94.47	96.83	94.47	94.47	94.47
120	Optimal dose (g)	0.9	1.2	0.95	1.2	0.95	1.25	1	1.25	1.05	1.25	1.1	1.25
	Target attainment (%)	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	83.68	74.41	81.15	74.41	78.44	70.44	76.09	70.44	74.41	70.44	70.44	64.62
	Cmin 48 ≤ 2.5 mg/L (%)	96.83	96.83	96.83	96.83	96.83	96.83	96.83	96.83	96.83	94.47	96.83	94.47
130	Optimal dose (g)	0.9	1.3	0.95	1.3	1	1.3	1	1.3	1.05	1.3	1.1	1.3
	Target attainment (%)	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	92.07	77.08	83.68	76.09	81.15	74.41	81.15	70.44	77.08	70.44	74.41	70.44
	Cmin 48 ≤ 2.5 mg/L (%)	99.28	96.83	96.83	96.83	96.83	96.83	96.83	96.83	96.83	96.83	96.83	96.83
140	Optimal dose (g)	0.9	1.35	0.95	1.4	1	1.4	1.05	1.4	1.05	1.4	1.1	1.4
	Target attainment (%)	92.01	92.25	92.01	92.25	92.01	92.25	93.28	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	92.07	78.44	92.07	77.08	83.68	76.09	81.15	74.41	81.15	74.41	77.08	70.44
	Cmin 48 ≤ 2.5 mg/L (%)	100	96.83	99.28	96.83	96.83	96.83	96.83	96.83	96.83	96.83	96.83	96.83
150	Optimal dose (g)	0.9	1.45	0.95	1.45	1	1.45	1.05	1.45	1.05	1.45	1.1	1.45
	Target attainment (%)	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	94.47	78.44	93.56	78.44	92.07	78.44	83.68	77.08	83.68	76.09	81.15	74.41
	Cmin 48 ≤ 2.5 mg/L (%)	100	96.83	100	96.83	100	96.83	99.28	96.83	96.83	96.83	96.83	96.83
160	Optimal dose (g)	0.95	1.5	0.95	1.5	1	1.55	1.05	1.55	1.1	1.55	1.1	1.55

	Target attainment (%)	93.28	92.25	92.01	92.25	92.01	92.25	92.01	92.25	93.28	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	94.47	83.68	94.47	78.44	93.56	78.44	92.07	78.44	87.99	77.08	83.68	76.09
	Cmin 48 ≤ 2.5 mg/L (%)	100	96.83	100	96.83	100	96.83	100	96.83	99.28	96.83	99.28	96.83
170	Optimal dose (g)	0.95	1.6	0.95	1.6	1	1.6	1.05	1.6	1.1	1.6	1.1	1.6
	Target attainment (%)	93.28	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	94.47	83.68	94.47	83.68	94.47	78.44	93.56	78.44	92.07	78.44	92.07	77.08
	Cmin 48 ≤ 2.5 mg/L (%)	100	96.83	100	96.83	100	96.83	100	96.83	100	96.83	100	96.83
180	Optimal dose (g)	0.95	1.65	1	1.65	1	1.65	1.05	1.7	1.1	1.7	1.15	1.7
	Target attainment (%)	93.28	92.25	93.28	92.25	92.01	92.25	92.01	92.25	92.01	92.25	93.28	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	96.83	89.62	94.47	87.99	94.47	83.68	94.47	78.44	93.56	78.44	93.56	78.44
	Cmin 48 ≤ 2.5 mg/L (%)	100	96.83	100	96.83	100	96.83	100	96.83	100	96.83	100	96.83
190	Optimal dose (g)	0.95	1.75	1	1.75	1.05	1.75	1.05	1.75	1.1	1.75	1.15	1.75
	Target attainment (%)	93.28	92.25	93.28	92.25	93.28	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	96.83	92.07	96.83	89.62	94.47	87.99	94.47	83.68	94.47	78.44	93.56	78.44
	Cmin 48 ≤ 2.5 mg/L (%)	100	96.83	100	96.83	100	96.83	100	96.83	100	96.83	100	96.83
200	Optimal dose (g)	0.95	1.8	1	1.8	1.05	1.8	1.05	1.8	1.1	1.8	1.15	1.85
	Target attainment (%)	93.28	92.25	93.28	92.25	93.28	92.25	92.01	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	96.83	92.07	96.83	92.07	96.83	89.62	96.83	87.99	94.47	83.68	94.47	78.44
	Cmin 48 ≤ 2.5 mg/L (%)	100	99.28	100	99.28	100	96.83	100	96.83	100	96.83	100	96.83
210	Optimal dose (g)	0.95	1.9	1	1.9	1.05	1.9	1.1	1.9	1.1	1.9	1.15	1.9
	Target attainment (%)	92.01	92.25	93.28	92.25	93.28	92.25	93.28	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	96.83	92.07	96.83	92.07	96.83	92.07	96.83	89.62	96.83	87.99	94.47	80.97
	Cmin 48 ≤ 2.5 mg/L (%)	100	99.28	100	99.28	100	99.28	100	96.83	100	96.83	100	96.83

220	Optimal dose (g)	0.95	1.95	1	1.95	1.05	1.95	1.1	1.95	1.1	1.95	1.15	1.95
	Target attainment (%)	92.01	92.25	93.28	92.25	93.28	92.25	93.28	92.25	92.01	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	96.83	93.56	96.83	93.56	96.83	93.56	96.83	92.07	96.83	89.62	96.83	87.99
	Cmin 48 ≤ 2.5 mg/L (%)	100	100	100	100	100	99.28	100	99.28	100	99.28	100	96.83
230	Optimal dose (g)	1	2	1	2	1.05	2.05	1.1	2.05	1.15	2.05	1.15	2.05
	Target attainment (%)	93.28	92.25	92.01	92.25	93.28	92.25	93.28	92.25	93.28	92.25	92.01	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	96.83	93.56	96.83	93.56	96.83	93.56	96.83	93.56	96.83	89.62	96.83	89.62
	Cmin 48 ≤ 2.5 mg/L (%)	100	100	100	100	100	100	100	100	100	99.28	100	99.28
240	Optimal dose (g)	1	2.1	1.05	2.1	1.05	2.1	1.1	2.1	1.15	2.1	1.2	2.1
	Target attainment (%)	93.28	92.25	93.28	92.25	92.01	92.25	93.28	92.25	93.28	92.25	93.28	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	96.83	93.56	96.83	93.56	96.83	93.56	96.83	93.56	96.83	93.56	96.83	91.1
	Cmin 48 ≤ 2.5 mg/L (%)	100	100	100	100	100	100	100	100	100	100	100	100
250	Optimal dose (g)	1	2.15	1.05	2.15	1.05	2.15	1.1	2.15	1.15	2.15	1.2	2.15
	Target attainment (%)	93.28	92.25	93.28	92.25	92.01	92.25	93.28	92.25	93.28	92.25	93.28	92.25
	Cmin 24 ≤ 2.5 mg/L (%)	96.83	94.47	96.83	93.56	96.83	93.56	96.83	93.56	96.83	93.56	96.83	93.56
	Cmin 48 ≤ 2.5 mg/L (%)	100	100	100	100	100	100	100	100	100	100	100	100