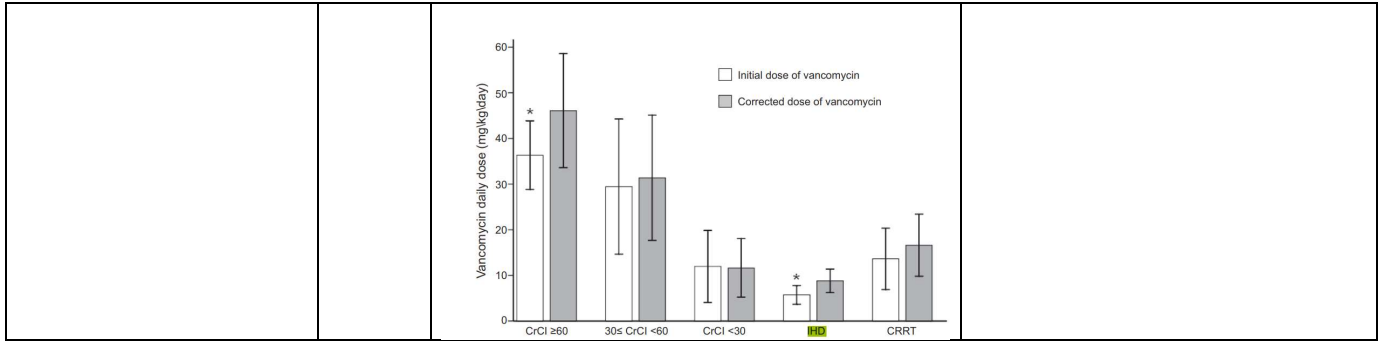


Clcr = creatinineklaring, CRRT = continue nierfunctie vervangende therapie, CVVH = continu venoveneuze hemofiltratie, CVVHD = continu venoveneuze hemodialyse, CVVHDF = contrinu venoveneuze hemodiafiltratie. GFR = glomerulaire filtratie snelheid, HDF = hemodiafiltratie IHD = intermitterende hemodialyse, ke = eliminatiesnelheidsconstante, Scr = serumcreatinine

Onderbouwend	Bewijs	Effect	Opmerkingen
Petejova N ea. Vancomycin removal during low-flux and high-flux extended daily hemodialysis in critically ill septic patients. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2012;156:342-7.	2	<p>Patiënten met sepsis en acuut nierfalen ondergingen dagelijks 6 uur hemodialyse met een low-flux membraan (n=5) of een high-flux membraan (n=4). In het laatste uur van de dialyse werd vancomycine toegediend.</p> <p>Mediane dosis dag 1: 10.6 mg/kg Mediane dosis dag 2: 11.0 mg/kg Predialyse targetconcentratie: 10-20 mg/l.</p> <p>Low-flux membraan: 17% (8-38%) vancomycine werd verwijderd High-flux membraan: 31% (13-43%) vancomycine werd verwijderd.</p> <p>High-flux dag 1: T1/2: off-dialyse 28 h; on-dialyse 11 h Cl: off-dialyse 14 ml/min; on-dialyse 50 ml/min Low-flux dag 1: T1/2: off-dialyse 19 h; on-dialyse 18 h Cl: off-dialyse 26 ml/min; on-dialyse 41 ml/min High-flux dag 2: T1/2: off-dialyse 39 h; on-dialyse 7 h Cl: off-dialyse 8 ml/min; on-dialyse 60 ml/min Low-flux dag 2: T1/2: off-dialyse 35 h; on-dialyse 17 h Cl: off-dialyse 9 ml/min; on-dialyse 29 ml/min</p>	<p>Auteurs: Both high-flux and low-flux membrane dialysis remove considerable amounts of vancomycin in critically ill septic patients with AKI. Application of vancomycin after each dialysis was required to maintain therapeutic concentrations.</p> <p>During the 3-6 h following high-flux dialysis, blood concentrations of vancomycin rebound by 16-36%, reflecting a redistribution phase.</p> <p>An AUC₀₋₂₄/MIC ratio ≥ 400 was achieved in only 3 out of 9 patients on both study days.</p> <p>In eight of nine patients vancomycin had already been administered before inclusion in the study.</p>
Chaijamorn W. ea. Vancomycin clearance during continuous venovenous haemofiltration in critically ill patients. Int J Antimicrob Agents. 2011;38:152-6	2	<p>Patiënten die CVVH ondergingen (n=7) kregen 1000 mg vancomycine i.v. in 2 uur.</p> <p>Sieving coefficient: 0.71 Cl_{CVVH}: 12 ml/min. (= 49% van de totale klaring, net als het aandeel non-renale klaring) 214 mg (= 21%) van de vancomycinedosis verwijderd na 12 uur CVVH. T_{1/2}: 12 uur</p>	<p>Auteurs: The maintenance dose of vancomycin calculated from parameters from patients in this study, would be 500–750 mg every 12 h to provide a steady-state trough concentration of 15–20 mg/L.</p>
Chung J ea. Optimal dose of vancomycin for treating methicillin-resistant Staphylococcus aureus pneumonia in critically ill patients. Anaesth. Intensive Care 2011;39: 1030-37.	2	<p>CrCl < 30 ml/min (IDH) (n=8): t_{1/2} 34.4 uur Cl 81% afname, dalspiegel 7.4 mg/l; CrCl < 30 ml/min (CRRT) (n=17): t_{1/2} 22.9 uur, Cl 64% afname, dalspiegel 15.2 mg/l; tov patiënten met Clcr > 60 ml/min (n=50); t_{1/2} 7.2 uur, dalspiegel 12.5 mg/l).</p> <p>Patiënten met pneumonie werden behandeld met een initiële dosis vancomycine i.v. 1000 mg elke 12 uur. Vervolgens werd de dosering aangepast obv de nierfunctie: CrCl <30 ml/min (IDH): 1 g elke 72-96 uur. CrCl <30 (CRRT): 500 mg-1 g elke 24 uur.</p>	<p>Auteurs: A higher dose of vancomycin is necessary to maintain a serum trough concentration of between 15 to 20 mg/l, particularly in critically ill patients with CrCl above 60 ml/minute or those on IHD. However, we did not observe a significant association between vancomycin serum trough concentrations and treatment outcomes.</p>



Overig	Opmerkingen
<p>SPC vancomycine Aurobindo 27-01-22.</p>	<p>Vancomycine is slecht dialyseerbaar via intermitterende hemodialyse. Het gebruik van hogefluxmembranen en continue niervervangende therapie (CRRT) verhoogt echter de klaring van vancomycine en vereist doorgaans een vervangende dosering (gewoonlijk na de hemodialysesessie in geval van intermitterende hemodialyse).</p> <p>De gebruikelijke startdosis voor volwassen patiënten is 15 tot 20 mg/kg die elke 24 uur kan worden toegediend bij patiënten met een creatinineklaring tussen 20 en 49 ml/min. Bij patiënten met een ernstig verminderde nierfunctie (creatinineklaring lager dan 20 ml/min) of patiënten die niervervangende therapie ondergaan, zijn de juiste timing en de hoeveelheid van volgende doses sterk afhankelijk van de modaliteit van de RTT en moeten ze gebaseerd zijn op de dalserumconcentraties vancomycine en op de restnierfunctie. Afhankelijk van de klinische situatie, moet worden overwogen om, in afwachting van de resultaten van de vancomycineconcentraties, de volgende dosis voorlopig niet te geven.</p> <p>Bij de kritiek zieke patiënt met nierinsufficiëntie moet de eerste opladdosis (25 tot 30 mg/kg) niet worden verlaagd</p> <p>Bij patiënten die intermitterende hemodialyse ondergaan, worden de vancomycineconcentraties gewoonlijk verkregen vóór het begin van de hemodialysesessie.</p> <p>Hoewel vancomycine niet efficiënt wordt geëlimineerd door hemodialyse is er wel eens een toename van de vancomycineklaring gemeld met hemoperfusie en hemofiltratie.</p>
<p>Rybak MJ ea. Therapeutic monitoring of vancomycin for serious methicillin-resistant Staphylococcus aureus infections: A revised consensus guideline and review by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the Society of Infectious Diseases Pharmacists Am J Health-Syst Pharm. 2020;77:835-864.</p>	<p>These are the consensus statements and guideline of ASHP, IDSA, the Pediatric Infectious Diseases Society (PIDS), and SIDP.</p> <p>Loading doses are recommended in patients who are critically ill or in the ICU, require dialysis or renal replacement therapy.</p> <p>Recommendation 10: In order to achieve rapid attainment of targeted concentrations in critically ill patients with suspected or documented serious MRSA infection, 20 to 35 mg/kg (max. 3000 mg) can be considered for intermittent-infusion administration.</p> <p>IHD</p> <p>Many dialysis-related factors affect the degree of vancomycin exposure in these patients. These considerations include the amount of time between vancomycin dose administration and the scheduled time of the next dialysis session, whether the dose is given during dialysis or after hemodialysis has ended, and the dialyzer's permeability if the dose is administered intradiallytically. Dialysis frequency also plays a role in dosing decisions.</p> <p>Recommendations:</p> <p>The following tabulation outlines recommended vancomycin loading and maintenance doses for patients receiving hemodialysis, with accounting for permeability of the dialyzer and whether the dose is administered intradiallytically or after dialysis ends (B-II).</p>

Timing and Dialyzer Permeability	Vancomycin Dose, mg/kg ^a	Timing and Dialyzer Permeability	Vancomycin Dose, mg/kg ^a
After dialysis ends		Intradialytic	
Low permeability	Loading: 25 Maint.: 7.5 ^b	Low permeability	Loading: 30 Maint.: 7.5-10 ^b
High permeability	Loading: 25 Maint.: 10 ^b	High permeability	Loading: 35 Maint.: 10-15 ^b

^aFrom references 104, 129, 130, 137, 138, 140, and 147.

^bThrice-weekly dose administration.

Since efficacy data are unavailable for AUC values of < 400mg.h/L, monitoring based on predialysis serum concentrations and extrapolating these values to estimate AUC is most practical. Maintaining predialysis concentrations between 15 and 20 mg/L is likely to achieve the AUC of 400 to 600 mg·h/L in the previous 24 hours (C-III). Predialysis serum concentration monitoring should be performed not less than weekly and should drive subsequent dosing, as opposed to a strict weight-based recommendation, although these recommended doses provide a useful starting point until serum concentrations have been determined (B-II).

CRRT

Loading doses of 20 to 25 mg/kg by actual body weight should be used in patients receiving CRRT at conventional, KDIGO-recommended effluent rates of 20 to 25 ml/kg/h (B-II). Initial maintenance dosing for CRRT with effluent rates of 20 to 25 ml/kg/h should be 7.5 to 10 mg/kg every 12 hours (B-II). Maintenance dose and dosing interval should be based on serum concentration monitoring, which should be conducted within the first 24 hours to ensure AUC/MIC targets are met. In fluid overloaded patients, doses may be reduced as patients become euvolemic and drug Vd decreases. The use of CI vancomycin in patients receiving CRRT appears to be growing, and this method could be used in place of intermittent vancomycin dosing, especially when high CRRT ultrafiltrate/dialysate flow rates are employed (B-II).

Westra N ea.
Vancomycin pharmacokinetic model development in patients on intermittent online hemodiafiltration. PLoS One. 2019;14:e0216801.

Two-compartment PPK models were developed using data from HDF patients (n = 17). Data from LF (low flux)-HD patients (n=21) was used to evaluate the model. All patients were dialyzed over a period of 4 hours.

Table 3. Dosing regimen for administering vancomycin during HDF and LF-HD using a dosing interval of 48 h.

	infused during last 60 min			Infused during last 60 min			Infused during last 30 min		
	Extracorporeal bloodflow (mL/min)			Extracorporeal bloodflow (mL/min)			Extracorporeal bloodflow (mL/min)		
	200	250	300	200	250	300	200	250	300
Weight (kg)	Loading dose (mg)			Maintenance doses (mg)					
50	1300	1300	1400	700	800	800	700	700	700
60	1500	1500	1500	700	700	800	700	700	700
70	1600	1700	1700	700	700	800	700	700	700
80	1700	1700	1700	700	700	800	700	700	700
90	1800	1800	1800	700	700	800	700	700	700
100	1800	1900	1900	700	700	800	700	700	700
110	1900	1900	1900	700	700	800	700	700	700
120	2000	2000	2000	700	700	800	700	700	700

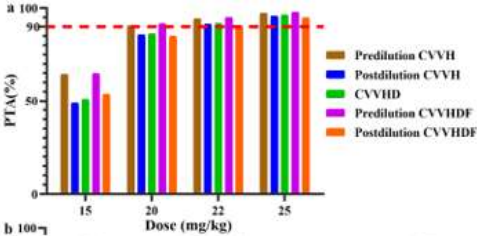
The dosing regimen is based on infusion during the final 60 min versus the final 30 min of HDF and LF-HD for different weight classes and different extracorporeal bloodflows to achieve AUC_{24h} ≥ 400 mg·h/L. Vancomycin dosages were rounded up to a multiple of 100 mg. This dosing regimen for dosing vancomycin is applicable to HDF and LF-HD patients.

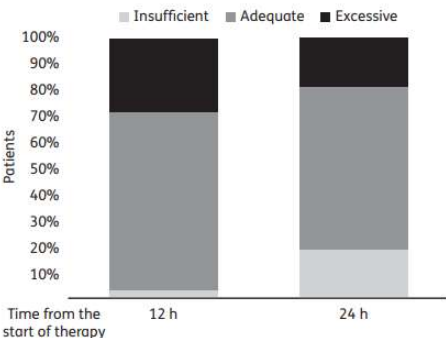
Table 4. Dosing regimen for administering vancomycin during HDF and LF-HD using a dosing interval of 72 h.

	infused during last 60 min			Infused during last 60 min			
	Extracorporeal bloodflow (mL/min)			Extracorporeal bloodflow (mL/min)			
	200	250	300	200	250	300	
Weight (kg)	Loading dose (mg)			Maintenance doses (mg)			We
50	1700	1700	1700	1000	1000	1100	50
60	1800	1800	1800	1000	1000	1000	60
70	1900	2000	2000	1000	1000	1000	70
80	2000	2000	2000	1000	1000	1000	80
90	2100	2100	2100	1000	1000	1000	90
100	2100	2100	2200	1000	1000	1000	100
110	2200	2200	2200	1000	1000	1000	110
120	2200	2300	2300	1000	1000	1000	120

The dosing regimen is based on infusion during the final 60 min of HDF and LF-HD for different weight classes and different extracorporeal blood flows to achieve AUC_{24h} ≥ 400 mg·h/L. Vancomycin dosages were rounded up to a multiple of 100 mg. This dosing regimen for dosing vancomycin is applicable to HDF and LF-HD patients.

Auteurs: In both HDF and LF-HD the optimal vancomycin loading dose for a typical patient weighing 70 kg is 1700 mg when administered during the last 60 minutes of the hemodialysis session. Maintenance dose is 700 mg if administered during the last 30 or 60 minutes of the hemodialysis session.

<p>Chen J ea. Optimizing antimicrobial dosing for critically ill patients with mrsa infections: a new paradigm for improving efficacy during continuous renal replacement therapy. pharmaceuticals. 2022;14:842.</p>	<p>Monte Carlo simulation for 10,000 replicates was applied to identify the optimal regimens of antimicrobial agents in patients with methicillin-resistant <i>Staphylococcus aureus</i> (MRSA) infections based on the mechanisms of different CRRT modalities on drug clearance. A PubMed search was conducted to collect the parameters for vancomycin.</p> <p>$C_{min} \geq 15$ mg/L was used as the target for optimizing the loading dose, and $AUC_{0-24}/MIC \geq 400$ was used for optimizing the maintenance dose.</p> <ul style="list-style-type: none"> A vancomycin loading dose of 20 mg/kg achieved the target in five CRRT modalities.  <p>Figure 1. The probability of target attainment (PTA) values of antimicrobial agents in loading doses for patients undergoing different continuous renal replacement therapy modalities. The red dashed horizontal line indicates 90% PTA. (a)—Vancomycin;</p> <ul style="list-style-type: none"> The simulation results indicated that the CRRT modality (CVVH, CVVHD and CVVHDF) had little effect on PTA values. For MIC was 1 mg/L, the PTA values were >90% under the dosage regimen of 0.5 g every 8 h in five CRRT modalities. The standard dosage regimen of 1 g every 12 h afforded PTA values >90% only for $MIC \leq 1$ mg/L. The vancomycin dosage regimen of 0.5 g every 8 h achieved cumulative fraction of response values >90% regardless of CRRT modality. The vancomycin dosage regimens under a CRRT dose of 25–30 mL/kg/h were similar to those under the reference CRRT dose (22.0 ± 6.1 mL/kg/h). When a higher CRRT dose of 35 mL/kg/h was prescribed, the vancomycin dosage regimen needed to increase to 1 g every 12 h and 2 g every 12 h at MIC of 1 mg/L and 2 mg/L, respectively. <p>Auteurs: this study indicated that the vancomycin loading dose regimen of 20 mg/kg followed by 0.5 g every 8 h could achieve the PK/PD target for MRSA under five different CRRT modalities with a CRRT dose</p> <p>Results suggested that a dosage regimen of 1 g every 8 h could obtain an optimal PTA value when MIC was 2 mg/L. However, the C_{min} estimated values of this regimen under five modalities were 41.0, 36.7, 29.8, 33.1, and 32.0 mg/L, which were higher than the therapeutic window for vancomycin (10–20 mg/L). Therefore, vancomycin was not recommended for treating MRSA when the MIC was 2 mg/L</p>
<p>Smeets TJL, ea. Vancomycine bij intensiecare-patiënten met continue dialyse. Nederlands Platform voor Farmaceutisch Onderzoek. 2022;7:a1750.</p>	<p>$Cl_{CVVHD_{citraat}}$ (n=13): 61.5%; $Cl_{CVVHD_{overig}}$ (n=5): 40%; Cl_{CVVHDF} (n=2): 50%</p> <p>van de patiënten had een vancomycine concentratie ≥ 20 mg/l 24 uur na start toediening. De mediane oplaaddosering en dagdosering was respectievelijk 20 mg/kg en 1008 mg/dag.</p> <p>$Cl_{CVVHD} = 25.3$ ml/min $Cl_{CVVHDF} = 37,2$ ml/min $Cl_{restnierfunctie} = 1,7$ ml/min (= 7.4% van de totale klaring)</p> <p>Prospectief, observationeel, farmacokinetiek onderzoek.</p> <p>Auteurs: De startdosering van vancomycine tijdens CRRT-behandeling bij IC-patiënten resulteert bij 50% van de onderzochte patiënten tot een te lage vancomycineconcentratie 24 uur na start van de toediening. Dit onderzoek laat zien dat optimalisatie van de startdosering van vancomycine nodig is tijdens CRRT-behandeling. Onder andere dialysaatflow en restnierfunctie hebben invloed op de hoogte van de vancomycinespiegel.</p>

<p>Roberts JA ea. The effect of renal replacement therapy and antibiotic dose on antibiotic concentrations in critically ill patients: data from the multinational sampling antibiotics in renal replacement therapy study. Clin Infect Dis. 2021;72:1369–78.</p>	<p>Prospective, observational, multinational, pharmacokinetic study. Patients received CVVH, CVVHD, CVVHDF or PIRRT (prolonged intermittent RRT). The study antibiotic dose and administration was determined by the treating clinical team. The antibiotic dosing regimens showed a daily dose variation of 4-fold for vancomycin (960 mg every 24 h – 2000 mg every 12 h). median trough concentrations vancomycine: CRRT (n=28): 18 mg/L PIRRT (n=32): 15 mg/L Trough concentrations failed to meet optimal higher limits (>20 mg/L) in 72% and optimal lower (>15 mg/L) 55% of patients for vancomycin.</p>
<p>Kirwan M ea. Exploring population pharmacokinetic models in patients treated with vancomycin during continuous venovenous haemodiafiltration (CVVHDF). Crit Care. 2021;25:443.</p>	<p>Retrospective population pharmacokinetic analysis of PK of vancomycin following intermittent infusion in critically ill patients receiving CVVHDF. A total of 106 vancomycin dosing intervals (155 levels) in 24 patients were examined. An acceptable 1-compartment base model was produced. Auteurs: PTA simulations suggest that acceptable trough vancomycin concentrations (target concentrations are 15–20 mg/L) can be achieved early in treatment with a 2 g loading dose and maintenance dose of 750 mg 12 hourly for critically ill patients on CVVHDF.hall</p>
<p>Goti V. ea. hospitalized patients with and without hemodialysis have markedly different vancomycin pharmacokinetics: a population pharmacokinetic model-based analysis. Ther Drug Monit. 2018;40:212-21.</p>	<p>PPK-model gemaakt op basis van retrospectieve data van 1812 patiënten. 336 hiervan ondergingen hemodialyse. Clearance in patients undergoing hemodialysis was approximately 65% of the clearance in nondialysis patients, and the Vc in hemodialysis patients was approximately 50% lower compared to the Vc nondialysis patients. The steady-state volume of distribution (Vc + Vp) was 1.4 and 1.0 L/kg in the nondialysis and dialysis patient populations, respectively. Optimal loading dose for nondialysis patients: 25 mg/kg. Optimal loading dose dialysis patients: 15 mg/kg. Mean optimal maintenance dose nondialysis patients: 25.3 mg/kg/day Mean optimal maintenance dose dialysis patients: 6.7 mg/kg/day The optimized dosing resulted in 47% of subjects to be in the 10–20 mg/L by the trough after the first dose.</p>
<p>Beumier M ea. A new regimen for continuous infusion of vancomycin during continuous renal replacement therapy. J Antimicrob Chemother. 2013;68:2859-65.</p>	<p>Prospective study in septic patients on CRRT. Oplaaddosering: 35 mg/kg gegeven in 4 uur gevolgd door 14 mg/kg/dag. Vancomycineconcentraties waren 4 uur (T1): 44 mg/l; 12 uur (T2): 27 mg/l; 24 uur (T3): 23 mg/l; na start van de vancomycine toediening. Cl 33 ml/min; AUC 652 mg/h/l Vancomycin concentrations were adequate (= 20-30 mg/l) in 22/32 patients (69%) at T2 and in 20/32 (63%) at T3.</p>  <p>Figure 1. The proportion of patients with insufficient (<20 mg/L), adequate (20–30 mg/L) or excessive (>30 mg/L) vancomycin concentrations 12 and 24 h from the start of therapy.</p> <p>Auteurs: This new vancomycin regimen allowed the rapid achievement of target drug concentrations in the majority of patients. CRRT intensity had an influence on vancomycin clearance.</p>

Importantly, slight dose adjustments were necessary in 37% of patients at 24 h to correct either low (16–19 mg/L) or excessive (31–39 mg/L) drug concentrations. The intensity of CRRT significantly predicted total drug CL in our PK model. Finally, achievement of vancomycin concentrations (20–30 mg/L) that are associated with optimal PK/pharmacodynamics (i.e. AUC/MIC>400) were only useful for pathogens with a vancomycin MIC up to 1.5 mg/L.

Covajes C ea. Continuous infusion of vancomycin in septic patients receiving continuous renal replacement therapy. *Int J Antimicrob Agents.* 2013;41:261-6.

Retrospectieve studie. Data van volwassen patiënten die tenminste 48 h vancomycine kregen tijdens CRRT.

Table 3

Characteristics of vancomycin therapy (n = 85).

Characteristic	Data ^a
Duration of therapy (days)	4 [3–7]
Dose (mg/kg)	
Loading dose	16.4 ± 6.4
Day 1	23.5 ± 8.1
Day 2	23.2 ± 7.4
Day 3	23.3 ± 11.0
Vancomycin concentration (µg/mL)	
Day 1	24.7 ± 9.0
Day 2	26.0 ± 8.1
Day 3	27.7 ± 9.3
Delay to target concentrations (days)	1 [1–2]

^a Data are expressed as median [interquartile range] or mean ± standard deviation.

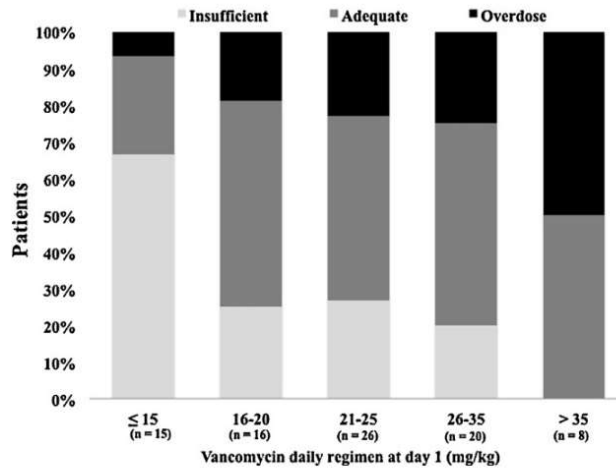


Fig. 2. Proportion of patients with inadequate (<20 µg/mL), adequate (20–30 µg/mL) and excessive (>30 µg/mL) vancomycin concentrations on the first day of therapy according to the daily vancomycin regimen (mg/kg).

Auteurs: Standard vancomycin doses of 16–35 mg/kg/day are adequate in most critically ill patients treated with a continuous infusion of vancomycin during CRRT. However, drug prescription should take into account the intensity of CRRT.

Vijsel LM ea. Initial vancomycin dosing recommendations for critically ill patients undergoing continuous venovenous hemodialysis. 2010, 63, 196-206.

Retrospectieve studie in ernstig zieke patiënten (n=24) die vancomycine kregen en CVVHD ondergingen.

CI: 40 ml/min; t1/2: 22 h

Table 4. Monte Carlo Simulation of Dosing Recommendations for Intermittent IV Infusions of Vancomycin

Regimen	Predicted Certainty (%)			
	Trough 15–20 mg/L	Trough < 12 mg/L	Trough > 25 mg/L	AUC _{24h} /MIC ≥ 400*
1 g q24h	12	51	19	52
1.25 g q24h	13	41	27	63
1.5 g q24h	13	34	35	71
1.75 g q24h	12	28	42	78
2.0 g q24h	11	24	48	83
15 mg/kg q24h	12	43	26	71
10 mg/kg q24h	10	60	14	41

AUC_{24h} = area under the concentration–time curve over 24 h, MIC = minimum inhibitory concentration.

*MIC was assumed to have a normal distribution, with a range between 0.5 and 2 mg/L and a mean value of 1 mg/L, with 1 million iterations using Monte Carlo simulation.

Table 5. Monte Carlo Simulation of Dosing Recommendations for Continuous IV Infusions of Vancomycin

Regimen	Predicted Certainty (%)			
	C* 15–20 mg/L	C* < 12 mg/L	C* > 25 mg/L	AUC _{24h} /MIC ≥ 400†
1.5-g loading dose	24	13	30	NA
2-g loading dose	16	4	55	NA
1 g/24 h continuous infusion (42 mg/h)	16	29	31	52
1.25 g/24 h continuous infusion (52 mg/h)	15	20	43	63
1.5 g/24 h continuous infusion (62.5 mg/h)	13	13	53	71
20 mg/kg loading dose	21	14	36	NA
15 mg/kg per 24 h continuous infusion	15	23	40	59
25 mg/kg loading dose	16	7	52	NA
20 mg/kg per 24 h continuous infusion	13	13	55	72

AUC_{24h} = area under the concentration–time curve over 24 h, C* = concentration after loading dose or concentration at steady state (for continuous infusions), MIC = minimum inhibitory concentration.

†MIC was assumed to have a normal distribution with a range between 0.5 and 2 mg/L and a mean value of 1 mg/L, with 1 million iterations using Monte Carlo simulation.

The pharmacokinetic parameters for vancomycin indicated that initial intermittent IV dosing of 1.25–1.5 g q24h or 15 mg/kg q24h would be suitable. For continuous infusion, a 1.5-g IV loading dose followed by continuous infusion of 1–1.5 g IV over 24 h (42–62 mg/h) would be recommended. However, Monte Carlo simulation revealed that the probability of achieving desired concentrations between 15 and 20 mg/L with any of these initial regimens is low.

Auteurs: There was considerable variation in vancomycin pharmacokinetics in this patient population. The observations reported here raise concerns about the reliability of numerous empiric dosing recommendations derived from small pharmacokinetic studies in heterogeneous populations. Follow-up therapeutic drug monitoring is essential to ensure that concentrations remain within the target range.

Hui K ea.
Optimizing vancomycin dosage regimens in relation to high-flux haemodialysis. J Antimicrob Chemother. 2019;74:130-4.

PPK model using retrospective data collected from 48 vancomycin courses administered to patients (n = 37) receiving high-flux HD (HFHD). Target pre-haemodialysis concentrations usually between 15 and 20 mg/L. Optimized dosing schedule for patients receiving HFHD:
Loading dose: 30 mg/kg
Maintenance dose: 10 mg/kg; An additional dose of 500 mg or 1 g was administered 24 h after the LD if HFHD occurred 48–72 h post-LD; an additional dose of 500 mg or 1 g was administered 24 h after the loading dose if HFHD occurred 48–72 h post-loading dose.
Auteurs: commonly prescribed vancomycin dosage regimens are unlikely to afford an AUC_{24h}/MIC ≥ 400 for most patients. Our dose-optimized regimen afforded a PTA ≥ 90% on all days of therapy and achieved clinically acceptable pre-haemodialysis concentrations.

Economou CJP ea.
Population pharmacokinetics of vancomycin in critically ill patients receiving prolonged intermittent renal replacement therapy. Int J Antimicrob Agents. 2018;52:151-157.

PPK model based on observational pharmacokinetic study in ICU patients (n=11) receiving vancomycin and receiving prolonged intermittent renal replacement therapy (PIRRT).
Cl_{PIRRT}: 58 ml/min
Assuming an MIC of 1 mg/L and in the presence of a 12- h PIRRT treatment, a regimen of 25 mg/kg per day was associated with 72% likelihood of an AUC_{0–24h}/MIC > 400 and a 38% likelihood of an AUC_{0–24h} > 700 mg.h/L which on balance was considered to be an acceptable regimen for the first 24 h of treatment for an 80 kg patient.
Auteurs: we observed large pharmacokinetic variability. Empirically, weight-based doses that are appropriate for the duration of PIRRT, should be selected and supplemented with therapeutic drug monitoring.

Gonzalez-Martin G, ea.
Pharmacokinetics of vancomycin in patients with severely impaired renal function. Int J Clin Pharmacol Ther 1996;34:71-75.

Piekconcentratie 37.8-109.3 µg/ml (gem. 64.9) en dalconcentratie (na 7 dagen) 2.2-11.4 µg/ml (gem. 6.6) bij 8 patiënten met Cl_{cr} < 10 ml/min (5 hemodialyse) na éénmalig 1 gram vancomycine i.v.: t_{1/2} 131 uur; V_d 0.92 l/kg; Cl 0.1 ml/min/kg. 1.5-21.1% dosis verwijderd door hemodialyse. Doseeradvies auteurs: Cl_{cr} < 10 ml/min: 1 gram vancomycine elke 7 dagen; Cl_{cr} ≈ 10 ml/min: monitor spiegels elke 2-3 dagen na 1^e dosis, geef nieuwe dosis als serumconc. < 5 mg/ml.

Tan CC ea.
Pharmacokinetics of intravenous vancomycin in patients with end-stage renal failure. Ther

Toename t_{1/2} bij 6 patiënten met Cl_{cr} < 5 ml/min (4 met hemodialyse) in vergelijking met gezonde personen (waarden uit literatuur) na 500 mg vancomycine i.v. elke 7 dagen. Piek- en dalspiegels dichtbij aanbevolen waarden (aanbevolen piekconcentratie doorgaans 20-30 µg/ml, dalconcentratie 5 µg/ml): piek 2 patiënten zonder hemodialyse 17.2 µg/ml; dal 3.3 µg/ml. t_{1/2} 2 patiënten zonder hemodialyse: 107 uur. Vancomycine

Drug Monit 1990;12:29-34.	vrijwel niet verwijderd door hemodialyse. 'From our study it appears that 500 mg of vancomycin given every seven days is probably adequate treatment for MRSA infections in end-stage renal failure.'
Amodio MI ea. Prolonged elevation of vancomycin concentrations in a patiënt with end-stage renal disease (letter to ed.). South Med J 1990;83:77-8.	Hoge serumconcentraties gedurende lange tijd bij patiënt met hemodialyse na éénmalig 1 gram vancomycine i.v. Conc ($\mu\text{g/ml}$) dag 4: 37.7; dag 16: 23.2; dag 34: 14.1. $t_{1/2}$ bij deze patiënt ongeveer 1 maand, 5x langer dan gemiddelde $t_{1/2}$ bij hemodialyse. 'Our experience suggests that patients with end stage renal disease should have careful monitoring of vancomycin to assure therapeutic levels and optimize dosing.'
Matzke GR ea. Systemic absorption of oral vancomycin in patients with renal insufficiency and antibiotic associated colitis. Am J Kidney Dis 1987;IX(no 5):422-5.	Correlatie tussen dosis en serumconcentraties vancomycine bij 5 patiënten met verminderde nierfunctie (4 hemodialyse, 1 met Clcr 33 ml/min) na 4 dd 125-500 mg oraal vancomycine gedurende minimaal 3 dagen. Stijging serumconcentraties gedurende eerste 3-4 dagen therapie, daarna afvlakking. 'Routine monitoring of vancomycin serum concentrations in adult patients may not be necessary unless high doses (> 2g/day) or prolonged therapy (> 10 days) is required'.
Bryan CS ea. Safety of oral vancomycin in functionally anephric patients. Antimicrob Agents Chemother 1978;14:634-5.	Cmax laag (0.66 resp. 0.46 $\mu\text{g/ml}$) of niet detecteerbaar bij 5 hemodialysepatiënten na 4 dd 500 mg vancomycine ged. 16 dagen. Bij 2 gezonde personen Cmax 0 $\mu\text{g/ml}$. 'We conclude that oral vancomycin therapy is safe in functionally anephric patients. Monitoring of blood levels might be desirable when inflammatory bowel disease is present'

Risicogroep	
-------------	--

Opmerkingen:

- Werkgroep 31-5-2023:
IHD: Rybak is internationaal de meest gevolgde studie. In het being wil je dat iemand snel op spiegel is, dus is het belangrijk niet te laag te beginnen. Daarna kan gedoseerd worden op geleide van de spiegel.
CVVH: in de literatuur wordt veelal opgeladen met 25 mg/kg (Rybak 2020 en Chen 2022), de studie van Chen ea. laat zien dat 1500 mg/dag voor vrijwel alle modaliteiten PTA > 90% geeft bij MIC 1 mg/ml.

	Wijziging kinetiek	Effect dialyse	Actie	Datum
Beslissing werkgroep	Ja	Ja	Ja	31 mei 2023