

Vancomycin protocol for dosing and monitoring in adult ICU patients

Introduction:

Vancomycin is a glycopeptide antibiotic used for treatment of patients with suspected or proven invasive gram-positive infections, including MRSA. Monitoring is important to minimize vancomycin toxicity, nephrotoxicity and ototoxicity.

Loading dose (for critically ill patients ONLY):

- Loading dose does not increase the risk of nephrotoxicity
- Loading dose of 25 mg/kg recommended for all patients (using actual body weight, rounded to the nearest 250 mg increment)
- Maximum loading dose in the elderly is 2 grams
- In obese patients, loading dose is given up to a maximum single dose of 3 grams (actual body weight)
- Loading dose counts as the first dose and the next dose should be given based on the dosage interval

Vancomycin Loading Dose Recommended for all critically ill patients [2,3]	
Patient Weight	Loading Dose
35 - 44 kg	1000 mg
45 -54 kg	1250 mg
55-64 kg	1500 mg
65 - 74 kg	1750 mg
75-79 kg	2000 mg
80-119kg Or 120kg and eCrCl < 59ml/min	2500mg
120kg and eCrCl ≥60ml/min	3000mg “maximum”

Maintenance dose:

- Following the loading dose, maintenance dose is given after one dosing interval. It should be rounded to the nearest 250 mg.
- For obese patients, initial dosing should be based on actual body weight then adjusted based on serum vancomycin concentrations to achieve therapeutic levels.

Dosing in non-dialysis patients				
Creatinine Clearance ml/min	Actual Body Weight			
	<60 kg	60 to 79 kg	80 to 99 kg	≥100 kg
>90	1000mg every 12hrs	1500mg every 12hrs	1750mg every 12hrs	2000mg every 12hrs
50 to 90	750mg every 12hrs	1000mg every 12hrs	1250mg every 12hrs	1500mg every 12hrs
15 to 49	750mg every 24hrs	1000mg every 24hrs	1250mg every 24hrs	1500mg every 24hrs
<15 ^a	750mg	1000mg	1250mg	1500mg
^a Check vancomycin level 24 hours after loading dose, wait for level result. Once level is < 20mg/L start maintenance dose of 15mg/kg. Re-check level after 24 hours and only re-dose when level is < 20mg/L				

Dosing in dialysis patient	
Type of dialysis	Suggested doses
Hemodialysis (IHD)	1. Loading dose administered as above (25mg/kg) 2. For patients on thrice-weekly dialysis (every other day), administer vancomycin 10 mg/kg in the last one to two hours of each dialysis session. 3. vancomycin serum concentration should be obtained prior to the third dialysis session
Continuous Renal Replacement (CRRT)	CVVH: Loading dose of 15 to 25 mg/kg, followed by either 1000 mg every 48 hours or 10 to 15 mg/kg every 24 to 48 hours CVVHD: Loading dose of 15 to 25 mg/kg, followed by either 1000 mg every 24 hours or 10 to 15 mg/kg every 24 hours CVVHDF: Loading dose of 15 to 25 mg/kg, followed by either 1000mg every 24 hours or 7.5 to 10 mg/kg every 12 hours Note: Consider re-dosing patients receiving CRRT for vancomycin concentrations <10 to 15 mcg/ml Trough sampling Before 3rd or 4th dose, see TDM
Peritoneal dialysis (PD)	10 – 15 mg/kg, then dose by level. Trough sampling 24 hours after initial dose.

Continuous venovenous hemofiltration (CVVH), continuous venovenous hemodialysis (CVVHD), and continuous venovenous hemodiafiltration (CVVHDF).

Dilutions and rate of infusion:

a. Dilutions:

Reconstitute vancomycin vials with water for injection to a final concentration of 50 mg/ml. Reconstituted solution must be further diluted with at least 500 mg of vancomycin per 100 mL of a compatible diluent (sodium chloride 0.9% or dextrose 5%) prior to parenteral administration.

b. Approach to infusion:

It should be administered over 30 – 60 minutes for each 500 mg.

Dose	Administration
750mg	In 250ml NS or D5 Over 60mins
1000mg	In 250ml NS or D5 Over 60 mins
1250mg	In 250ml NS or D5 Over 90 mins
1500mg	In 500ml NS or D5 Over 90 mins
1750mg	In 500ml NS or D5 Over 120 mins
2000mg	In 500ml NS or D5 Over 120 -150 mins
NS = sodium chloride 0.9% D5 = dextrose 5%	

Vancomycin Therapeutic Drug Monitoring: “For patients whom therapy is expected to continue beyond 3 days”

• For patients NOT on dialysis:

A. Trough sampling:

- Troughs should be drawn 30 minutes prior to **4th dose** (prior to the 3rd dose for patients with dosing intervals > 24 hours).
- DO NOT withhold doses whilst waiting for a vancomycin level result unless renal impairment or suspected toxicity.
- Levels should NOT be taken from the site of the venous catheter where vancomycin has been administered
- Once the target vancomycin trough concentration is achieved, vancomycin serum trough concentrations and serum creatinine concentration should be monitored at least weekly for patients with invasive infection, clinical instability, renal dysfunction, or morbid obesity as well as for patients on concomitant nephrotoxins.

B. Trough target range:

- 15 to 20 mcg/mL for deep-seated infection, such as bacteremia, endocarditis, osteomyelitis, or pneumonia

C. Dose adjustment:

- Adjustment of the total daily dose with fixing the dosing interval, will result in proportional change in the trough concentration (when renal function is stable and steady state is reached). Dose adjustment should be done using the following equation:

$$\text{New TDD} = \frac{\text{Target trough level} \times \text{current TDD}}{\text{Current trough level}}$$

TDD= total daily dose

- If a dose alteration is made re-check trough level immediately prior to the 4th administration of the new dose.

When trough concentrations are > 5 mcg/mL above target range (>25mcg/ml):

- Subsequent vancomycin doses should be held
- Daily vancomycin levels should be repeated until the level is within the target range.
- New dosing regimen should be established based on the principles outlined above.

• For patients on dialysis:

➤ **IHD:**

- Trough sample should be taken prior the 3rd dialysis session following initiation of therapy
- Dose adjustment should be made as shown in “IHD dose adjustment table”
- Following dose adjustment, repeat vancomycin serum concentration should be measured prior to the following dialysis session.
- Once the pre-dialysis (tough) vancomycin concentration is within target range, it should be checked weekly.

➤ **CRRT:**

Trough sampling:

- if dosing intervals ≥ 24 hours, prior 3rd dose
- if dosing intervals <24 hours, prior 4th dose

➤ **PD:**

Trough sampling 24 hours after initial dose.

IHD dose adjustment	
Trough level	Intervention
<15 mcg/ml	Increase dose by 250 to 500mg
15 to 25 mcg/ml	No change in therapy
26 to 35 mcg/ml	Decrease dose by 250 to 500mg
>35 mcg/ml	Hold vancomycin dose, and repeat level prior to each subsequent dialysis session until it falls below 35mcg/ml Resume with dose reduction of 500 to 1000mg

Risk factors for nephrotoxicity: “Monitor creatinine daily”

- Acute renal failure attributable to vancomycin should prompt discontinuation of the drug
- Consider an alternative agent if creatinine is rising or the patient becomes oliguric.
- Risk factors for nephrotoxicity associated with vancomycin include:
Duration of therapy, presence of underlying renal dysfunction, critical illness, or concurrent use of other nephrotoxic agents: aminoglycosides, ACE inhibitors, NSAIDs, potent diuretics (furosemide), amphotericin B.

THIS PROTOCOL HAS BEEN DEVELOPED IN COLLABORATION BETWEEN THE PHARMACY, MICROBIOLOGY, NEPHROLOGY AND INTENSIVE CARE DEPARTMENTS