

Northwestern Lake Forest Hospital

Pharmacy Department Pharmacokinetic Services

March 2019

VANCOMYCIN INITIAL DOSING: 15-20mg/kg

- Based on actual body weight; Round to the nearest 500mg
- Maximum **individual** dose 2 grams/dose, Maximum **initial** total dose of 4 grams/day
- Consider loading dose (20-30mg/kg) for suspected bacteremia, endocarditis, osteomyelitis, meningitis, and hospital acquired pneumonia caused by *S. aureus*
- For patients with BMI ≥ 35 kg/m² consider using lower doses of 10-12.5mg/kg/dose (based on total body weight)

FREQUENCY OF DOSE BASED ON CrCL:

CrCl (ml/min)	Interval (Hours)
≥ 60	8-12
40-59	24
20-39	48
≤ 19	Random levels: re-dose at 15mg/kg when trough ≤ 15
Renal replacement therapy (non-PD)	15mg/kg Dose x1, then dose by levels(See Appendix A for level ordering)

PHARMACODYNAMIC TARGETS:

- Trough concentrations will be drawn to assist with AUC₂₄/MIC monitoring.
- Goal AUC₂₄/MIC is 400-600 for all indications.
- Trough concentrations should be measured 30 minutes prior to infusion of the 4th or 5th dose following the initial dose or dose adjustment. In the setting of suspected or confirmed acute kidney injury or early drug accumulation, a vancomycin trough may be obtained earlier than the 4th or 5th dose (but AUC₂₄/MIC monitoring will not apply).

DESIRED AUC₂₄/MIC: 400-600

- Same range for all indications
- Would recommend AUC₂₄/MIC closer to 400 for non-*Staphylococcus aureus* infections requiring vancomycin

CALCULATIONS:

- Assume fixed Vd: 0.7L/kg
- $C = \text{Dose}/Vd$
- Peak = measured vancomycin trough + C
- $K_{el} = [\ln(\text{peak}/\text{trough})]/\Delta\text{time}$
- $Cl = K_{el} * Vd$
- $AUC = \text{Dose (in 24h)}/Cl$

ABBREVIATIONS:

- Vd: volume of distribution
- C: concentration
- K_{el}: elimination rate constant
- Cl: clearance
- AUC: area under the curve

EXCLUSION CRITERIA (STANDARD DOSING USING DESIRED VANCOMYCIN TROUGH LEVELS): The following patient populations are excluded from AUC₂₄/MIC monitoring. It is recommended that these patients be monitored using vancomycin trough levels.

- Pediatric patients (age <18 years)
- Patients on renal replacement therapy (PD, iHD, SLED, CVVH, CVVHD, CVVDFH)
- Scr <0.5 mg/dL (if not clinically appropriate to round up)
- Vancomycin trough values <5 mcg/mL
- Confirmed CNS infections (may use AUC₂₄/MIC monitoring on a case by case basis)

Trough Levels: Recommend to be obtained when clinically necessary to assist with the following:

- Hemodialysis/Peritoneal Dialysis
- Fluctuating renal function
- Fluctuating fluid balance
- Invasive infection with prolonged course of vancomycin
- Suspected toxicity
- Morbid obesity
- Critically Ill patients
- Hemodynamic instability

DESIRED TROUGHS:

Goal Trough Level (mcg/ml)	Indication
<10	Not recommended for any indication, promotes resistance
10-15	Skin/soft tissue infections, non-CNS abscesses that have been drained
15-20	<ul style="list-style-type: none"> • Bacteremia • Endocarditis*** • Osteomyelitis/Prosthetic Joint • Hospital acquired pneumonia • Infections involving the CNS*** • Isolates with MIC > 1 mcg/ml

***May aim for higher troughs ~20 for these indications on a case by case basis. The remaining indications should aim for troughs to be closer to 15.

MONITORING/ DOSE ADJUSTMENT:

- Higher than targeted trough concentration: Increase dosing interval and/or reduction in dose. Reduction in dose will result in a proportional reduction in trough (assuming stable renal function)
- Lower than targeted trough concentration: Reduce the dosing interval and/or increase the dose. Increase in the dose will result in a proportional increase in trough (assuming stable renal function)
- If Redman's Syndrome occurs, extend time of infusion or prepare less concentrated product. You may also discuss pre-medication options with the provider.

Appendix A: Dosing of Vancomycin for Patients with Renal Replacement Therapy (RRT)

Prior to ordering levels please assess the following:

1. Determine RRT modality: intermittent hemodialysis (iHD), peritoneal dialysis (PD), or continuous renal replacement therapy (CRRT).
2. Determine if patient has any residual renal function (e.g., does the patient have any urine output?).
3. Administer appropriate loading dose based on actual body weight.
4. Random vancomycin levels will be used to guide subsequent dosing.

Intermittent Hemodialysis

- For patients on a stable, 3x weekly HD regimen (Mon/Wed/Fri, Tu/Th/Sa, etc.), obtain pre-HD levels. The following are pre-HD level goals based on infection severity/type:
 - For mild-to-moderate infections or non-deep-seated infections: goal 10-20 mcg/mL
 - For severe or deep-seated infections: goal 15-25 mcg/mL
 - See tables A and B on dosing recommendations based on pre-HD levels obtained or calculate vancomycin level
- For patients who are not on a stable HD regimen (daily HD, partial HD sessions, etc.), obtain post-HD levels. Please note, post-HD level must be obtained 3-4 hours after the conclusion of the HD session to account for re-distribution post-HD (otherwise, the level will appear falsely low). The following are post-HD level goals based on infection severity/type:
 - For mild-to-moderate infections or non-deep-seated infections: goal 10-15 mcg/mL
 - For severe or deep-seated infections: goal 15-20 mcg/mL
 - See tables C and D for dosing recommendations based on post-HD levels obtained or calculate vancomycin level
- Assumptions
 - Standard hemodialysis session removes ~30% of vancomycin
 - Quick calculation approach
 - Dose = Concentration Difference x Vd (where Concentration Difference is the Target Vancomycin Concentration – Current Vancomycin Concentration)
 - Vd = 0.7 L/kg x body weight (assuming population pharmacokinetics)

PRE-HD LEVELS

Table A: Maintenance Dosing for Mild to Moderate and Non-Deep-Seated Infections

Serum conc. of vancomycin (mcg/mL) Before HD	Maintenance Dose Given after HD
<10	1000 mg
10-20	500 mg
>20	Hold vancomycin

Table B: Maintenance Dosing for Severe Infections or Deep-Seated Infections

Serum conc. of vancomycin (mcg/mL) Before HD	Maintenance Dose Given after HD
<10	15mg/kg – round to the nearest 500 mg
10-20	7.5 mg/kg – round to the nearest 500 mg
20.1-25	500 mg
>25	Hold vancomycin

POST-HD LEVELS

Table C: Maintenance Dosing for Mild to Moderate and Non-Deep-Seated Infections

Serum conc. of vancomycin (mcg/mL) After HD	Maintenance Dose Given after HD
<10	1000 mg
10-15	500 mg
>15	Hold vancomycin

Table D: Maintenance Dosing for Severe Infections or Deep-Seated Infections

Serum conc. of vancomycin (mcg/mL) After HD	Maintenance Dose Given after HD
<10	1000 mg
10-20	500mg
>20	Hold vancomycin

Tables adapted from Crew et al. Vancomycin dosing and monitoring for patients with end-stage renal disease receiving intermittent hemodialysis. Am J Health-Syst Pharm. 2015;72:1856-64.

Peritoneal Dialysis

- For intravenous dosing (if systemic infection): 15-20 mg/kg loading dose, then by levels (goal 15-20 mcg/mL)
- For addition to peritoneal dialysate (for peritonitis alone):
 - Intermittent (once exchange per daily): 15-30 mg/kg IP every 5-7 days (supplemental doses may be needed for automatic peritoneal dialysis)
 - Continuous (mg/L, all exchanges): loading dose of 1000 mg/L IP, then 25 mg/L IP
- Keep serum vancomycin level >15 mcg/mL

References

Kam-Tao Li P, et al. ISPD peritonitis recommendations: 2016 update on prevention and treatment. Perit Dial Int. 2016;36(5):481-508.
 Kam-Tao Li P, et al. Peritoneal dialysis-related infections recommendations: 2010 update. Perit Dial Int. 2010;30:393-423.

Continuous Renal Replacement Therapy

- Determine CRRT modality.
- Determine total hourly effluent rate (pre-replacement fluid + post-replacement fluid + dialysate). Round to nearest whole number.
- Order vancomycin based on the following total effluent rates
 - 1 L/hr: anephric dose of vancomycin (15 mg/kg every 5 days) + 300 mg/day
 - 2 L/hr: anephric dose of vancomycin (15 mg/kg every 5 days) + 700 mg/day
 - 3 L/hr: anephric dose of vancomycin (15 mg/kg every 5 days) + 1000 mg/day
 - 4 L/hr: anephric dose of vancomycin (15 mg/kg every 5 days) + 1500 mg/day

References

Scheetz et al. Adjustment of antimicrobial dosages for continuous venovenous hemofiltration based on patient-specific information. Clin Infect Dis. 2006;42(3):436-437.
 Trotman et al. Antibiotic dosing in critically ill adult patients receiving continuous renal replacement therapy. Clin Infect Dis. 2005;41(8):1159-1166.