Northwestern Medicine®

INTRAVENOUS VANCOMYCIN USE IN ADULTS

Empiric vancomycin is often initiated to ensure adequate antibacterial coverage while awaiting culture results. The need to continue vancomycin, however, should be dependent on culture results confirming presence of an organism that requires vancomycin, such as methicillin-resistant *Staphylococcus aureus* (MRSA). Current vancomycin dosing guidelines recommend targets specific to serious MRSA infections. These particular targets are not validated for non-MRSA infections, and lower targets are recommended for other types of infections in most situations. This guidance is intended to maximize the appropriate use of and to minimize toxicity associated with vancomycin.

VANCOMYCIN TARGETS AND RECOMMENDATIONS BY INDICATION

[See details and dosing pearls below in the Dosing and Monitoring Section]

Clinical Scenario	Appropriate Use? (Y/N) If N, recommend D/C	Order levels* (Y/N)	Target AUC**	Recommendations
Bacteremia/Sepsis				
MRSA bacteremia	Y	Y	400-550	ID consult
Severe sepsis, unknown source	Y	N	N/A	If no MRSA isolated, discontinue vancomycin.
Single positive blood culture for gram positive cocci	Y	N	N/A	Should be discontinued once gram positive cocci identified as coagulase-negative Staph
Multiple (more than 1) positive blood cultures with Coag-neg staph or enterococci.	Y (possibly, if resistant to beta-lactams)	Y	<500	
Line related infection	Y	N	N/A	If no MRSA or clinically significant coag-neg Staph isolated, discontinue vancomycin.
Respiratory				
MRSA Pneumonia, documented	Y	Y	400-550	Consider switch to linezolid.
HAP/VAP, empiric	Y	N	N/A	Order MRSA nasal swab or BAL PCR; if negative, discontinue vancomycin.
CAP, empiric	Assess if high risk for MRSA using NM algorithm; if not high risk, vanco should be stopped.	N	N/A	If screening indicates patient is high risk, order MRSA nasal swab; if negative, discontinue vancomycin.

Skin/Skin Structure				
MRSA abscess	Y	Y	400-550	
Purulent cellulitis	Y	Y	<500	Significant risk of MRSA with purulent cellulitis; discontinue vancomycin if no MRSA isolated.
Non-purulent cellulitis	N			Vancomycin should not be used for non-purulent cellulitis. See NM skin/skin structure infection guidelines.
Bone/Joint				
MRSA osteomyelitis or joint infection	Y	Y	400-550	
Empiric for osteomyelitis or joint infection	Y (possibly, if high suspicion of MRSA and no positive cultures)	Y	<500	Long-term treatment with vancomycin in unconfirmed or non-MRSA infection should be focused on avoiding toxicity.
CNS				
Empiric for CNS infection	Y	Y	400-550	
Other				
Intra-abdominal infection (empiric)	N			MRSA not a significant cause of IAI.
UTI	Y (if MRSA)	N	N/A	ID consult should be obtained to define source of organism.

*If levels are not indicated due to indication, they can still be monitored to avoid toxicity in a patient who requires ongoing vancomycin therapy or whose renal function is worsening (per the clinical judgement of the pharmacist).). LEVELS SHOULD NOT BE ORDERED IN THE FIRST 48 HOURS OF THERAPY, as in these situations vancomycin may be discontinued.

**Clinical judgement should always be used in determining appropriate target AUC however the below clinical trial caveats should ALWAYS be applied when doing so

Data from the PROVIDE trial indicate that patients had better outcomes when AUC was <515 due to decreased toxicity noted.[3] Further evidence from the CAMERA 2 study suggests that a 24-hour AUC of 470 or greater has been associated with increased toxicity, indicating even lower AUCs may be necessary.[4] Please keep these thresholds in mind when monitoring vancomycin therapy and adjusting doses.

VANCOMYCIN DOSING AND MONITORING

General Vancomycin PK/PD Principles

Volume of distribution:

- Hydrophilic molecule
- Vd 0.7 L/kg is used; use adjusted body weight if obese, (ranges from 0.4-1L/kg)
- In obese patients:
    - Vd in obese patients 0.3-0.8 L/Kg of actual body weight (ABW)
    - 30% of adipose tissue contains water
    - Additional weight is due to increased adipose tissue, muscle mass, and connective tissue
    - Hypoalbuminemia may result in elevated free vancomycin concentrations

Empiric Vancomycin Dosing

- Dose based on actual body weight (ABW; including obese patients; max initial dose 2000 mg)
- Loading dose (20-25 mg/kg; max dose of 2000 mg) should be considered for the following situations:
    - Clinical instability
    - Documented severe MRSA infections
    - Suspected meningitis, endocarditis, or pneumonia
- Doses should be rounded to nearest 250 mg (e.g., 1000 mg, 1250 mg, 1500 mg, etc.)
- Maintenance dose and interval are based on renal function as determined by CrCl listed in Epic for clinically stable patients
- **Patients receiving vancomycin for surgical prophylaxis or group B strep prophylaxis are excluded from this empiric dosing guideline**

Creatinine Clearance (mL/min)	Initial Dose*
≥60	15 mg/kg Q12hr
~ 30-59	15-20 mg/kg 24hr
~ 21-29	15 mg/kg Q36hr
< 20**	15-20 mg/kg x 1 dose then dose by monitoring AUC

* Initial doses should be evaluated with consideration of the patient's clinical picture, and evaluation with a pharmacokinetic calculator is encouraged

**See below for initial dosing for ARF, HD, PD, or CRRT patients

Standard Dosing/Monitoring Procedure:

- One steady-state concentration (i.e., trough) will be obtained prior to the third or fourth dose ONLY WHEN CONCENTRATION MONITORING IS INDICATED. SEE TABLE ABOVE WHEN CONCENTRATION MONITORING IS NECESSARY.
    - Patients with acute renal failure or hemodynamic instability may need a level earlier
- Calculate vancomycin AUC using the Epic Kinetics Navigator (See Kinetics Navigator User Guide) or VancoPK.com.
- Target AUC is per above chart based on indication for vancomycin
- If hand calculation of AUC is needed, below are the calculations that will be used:

1. V_d= 0.7L/kg * ABW
    a. (use adj body weight if >130% IBW; adj body weight = IBW + 0.4[ABW-IBW])
2. C=Dose (mg; single dose) /Vd
3. Peak= vancomycin level + C (from above)
4. K_{el}= [ln(peak/trough)]/Δtime
5. CL= K_{el} x V_d
6. AUC= Dose (mg; in 24H period)/CL
    a. Ex. 1000mg q12H = 2000mg in 24H period
7. For dose adjustment, a simple proportional method can be used (i.e. if calculated AUC was 900 with 3000mg/day, a dose of 1500mg/day approximately correlates to an AUC of 450)

Definitions:
- V_d = Volume of distribution (L)
- ABW = Actual body weight (kg)
- IBW = Ideal body weight (kg)
- C = Concentration (mg/L)
- K_{el} = elimination rate constant (hr^{-1})
- CL = clearance (L/hr)
- Δtime = time from start of infusion to level collection (hr)
- AUC = Area under the curve (mg.h/L)

- Ongoing monitoring and follow-up levels:
    - Routine weekly concentration monitoring for patients with stable renal function IS NOT INDICATED.
    - Patients with a significant change in renal function (≥ 50% change or ≥ 0.3 mg/dL over 48 hr), clinical worsening, or hemodynamic instability should have concentration monitoring undertaken.
    - Lab Monitoring
        - Check SCr at least twice per week if feasible (more frequently if patient is an inpatient).
        - The pharmacist may order labs (e.g., SCr) per this protocol as needed to assess the patient for vancomycin monitoring.
    - **Dosing Pearls**:
        - Assessing clinical response and applying clinical judgement should always guide therapy adjustments. AUC calculations are just another tool to help with this assessment and blindly adjusting doses to achieve values in the "target range" is NEVER appropriate.
        - There is no demonstrated clinical benefit to a higher AUC if the patient is above 400 mg.h/L for severe MRSA patients; there is no need to increase the dose if this threshold is met.[3] No minimum AUC threshold has been established for non-MRSA patients.

DOSING AND MONITORING IN RENAL FAILURE PATIENTS

Dosing in Acute Renal Failure or Intermittent Hemodialysis

1. Give loading dose of 25 mg/kg x 1 dose (max 2 g)
2. The dosing pearls outlined above should always guide dose adjustments.
3. Check a vancomycin level at 24-48 hours post-dose or with am labs on the day of the next hemodialysis session (if applicable) to obtain an estimated steady state level
    a) High flux filters in HD will remove ~ 20-40% of the vancomycin dose during dialysis.
    b) Pre-dialysis vancomycin levels will be used for assessment (if applicable)
4. Redose with 10 mg/kg x 1 when level approaches or drops below 10 mcg/dL; redosing at a higher level may be necessary depending on infection severity/clinical status of patient
5. Should a post-dialysis level be required, the post-dialysis level should not be drawn less than 4 hours after completion of the dialysis session to allow time for redistribution of vancomycin post-dialysis.

Dosing in Continuous Renal Replacement Therapy

1. Give initial loading dose of 20-25 mg/kg per actual body weight (max 2 g) for patients receiving conventional effluent rates of 20-25 mL/kg/hr for CRRT
2. Maintenance dose of 15-20 mg/kg q24 hours is recommended for effluent rates of 20-25 mL/kg/hr

3. Serum concentrations should be drawn early in therapy (e.g., prior to the 2nd or 3rd dose), and the dose should be adjusted to maintain target level of 10-15 mcg/dL
4. Keep in mind potential CVVH line clotting, which may interrupt elimination of the vancomycin during the dosing interval.

Dosing in Peritoneal Dialysis

1. Give 25 mg/kg x 1 dose (max 2 g)
2. Check a vancomycin level at about 48 hours post-dose and repeat level as needed
3. Redose with 15 mg/kg when level reaches 10-15mcg/dL or just below
4. Continue checking levels at estimated time repeat dose will be due based on prior intervals to determine need to redose
5. Caveats of vancomycin use in peritoneal dialysis:
   - For treatment of peritoneal dialysis-related peritonitis, intraperitoneal vancomycin is recommended instead of intravenous due to inadequate concentrations in peritoneal fluid with systemic administration
   - Achievement of therapeutic targets in patients on peritoneal dialysis is difficult without high trough levels. Consider use of alternative agent in critically ill patients requiring vancomycin therapy, if possible.

References

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