Stanford Children's Health | Lucile Packard Children's Hospital Stanford

Guidelines for Vancomycin Use in Neonates and Children

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INDICATIONS

Vancomycin is appropriate for the following scenarios:

1. Suspected/Documented methicillin-resistant *S. aureus* or coagulase-negative staphylococcus infection
2. Infections due to ampicillin resistant, vancomycin susceptible *Enterococcus spp.*
3. Empiric treatment of *S. pneumoniae* meningitis
4. Perioperative prophylaxis in patients with MRSA/resistant gram-positive bacteria (GPB) colonization
5. Empiric therapy for febrile neutropenia with clinical instability or resistant bacteria suspected/documented

Vancomycin is NOT recommended for the following scenarios:

1. Continued empiric therapy if microbiologic testing does not confirm an infection due to a resistant GPB
2. Routine surgical prophylaxis
3. Treatment of beta-lactam susceptible GPB, e.g., MSSA, *Enterococcus spp.*, viridans group streptococci
4. Systemic or local prophylaxis for indwelling catheters
5. Infections due to *S. aureus* with MIC ≥2 µg/mL, consider alternative agent unless sputum culture

GOAL VANCOMYCIN EXPOSURE – AUC_{24} vs trough level

- **AUC_{24} of 400–600 mg*hr/L** is the best predictor of positive outcomes for **invasive MRSA** infection (assuming MIC ≤ 1 mg/mL by broth microdilution).
- AUC_{24} is predicted and estimated using the **InsightRX** via model-based Bayesian forecasting.

Target Vancomycin Area Under the Curve (AUC)

Indication	Suggested target	Considerations
Serious MRSA infections (including pneumonia, multifocal osteomyelitis, bacteremia)	AUC_{24} 400 – 600 mg*hr/L	**Troughs < 10 µg/mL may achieve this AUC_{24} goal**
Non-MRSA infections or cellulitis	AUC_{24} 400 – 600 mg*hr/L	Weak evidence to support an alternative target for non-MRSA infections; consider trough goals within 5 – 20 µg/mL depending on type of infection.

Important details

- Trough >15-20 µg/mL and AUC_{24} > 800 mg*hr/L is associated with AKI.
- AUC_{24} goal applies to renal replacement therapy (e.g., hemodialysis, CKRT) populations as well.
- CF sputum culture antibiotic susceptibility testing by E-test can report an MIC 1.5- to 2-fold higher than by broth microdilution; therefore, target AUC_{24}/MIC_{Etest} 200 – 400 mg*hr/L (minimum AUC_{24} of 400).
- Pediatric Infectious Diseases service may tailor the AUC_{24} target based on the infection and etiology.

INITIAL DOSING

- **Based on age, renal function, actual body weight, indication, and MIC, use InsightRX dosing platform to inform initial model-based dose recommendations in conjunction with clinical judgement.**
- Refer to the "Hemodialysis" or "Cardiac Surgical" vancomycin guidelines when applicable.
- Potential poor fit characteristics: concomitant nephrotoxins, critical illness (e.g., vasopressor requirement), CVICU, low muscle mass, obesity, renal replacement therapy, eGFR < 30 mL/min or fluctuating renal function
  - When the above characteristic(s) is/are present, consider conversative dosing with early TDM, e.g., prior to steady state
- Enter patient info in InsightRX for data collection purposes: hospital unit, indications, co-treatment options (e.g., HD, CKRT), co-morbidities (i.e., oncology, BMT, obese, low muscle mass)
- Consider historical, clinically relevant vancomycin regimens and levels to guide initial dose.
- Time 1st vancomycin dose based on recent doses received in the Emergency Dept. or outside hospital.
- Initial dosage range is 60 – 80 mg/kg/day divided every 6 to 8 hours for children > 3 months with normal renal function (max 3600 mg/day); use more conservative dosing and clinical judgement if poor fit characteristics are present, e.g., critical illness

THERAPEUTIC DRUG MONITORING (TDM)

- If stable patient, only perform TDM if anticipated duration of vancomycin therapy >48 hours, i.e., typically, no levels indicated for anticipated 48-hour rule-out.
- If unstable, critically ill patient (e.g., vasopressor required) or worsening renal function, perform TDM sooner (i.e., after first or second dose).
  - No requirement to be at 'steady-state' using InsightRX.
  - Strongly consider getting two concentrations within the same dosing interval to help improve PK estimates.
- Order levels to bundle and time with other blood draws preferred, 'random' levels may be ordered, unless poor fit characteristics present.
- Wait at least an hour after the end of the infusion if obtaining a random concentration.
- For "dose by level" or doses ≥24 hours apart (excluding stable neonates), perform TDM before each dose until stable dosing established.

DOSE ADJUSTMENT BASED ON TDM

- **Use InsightRX to inform model-based dose adjustments in conjunction with clinical judgement.**
  - Re-evaluate indication during review (e.g., new target, no longer indicated).
- Evaluate the probability of AUC_{24} >400 mg*hr/L (P_{AUC}) when determining dosing.
  - Goal to have P_{AUC} >80-90% which will require predicted $AUC_{24,ss} \approx 450$ mg*hr/L.
  - Balance P_{AUC} with probability of trough >20 µg/mL (P_{conc}). Goal P_{conc} <5-10%.
- Review 'Model Fit' indicator in InsightRX.
  - 'Intermediate' or 'Poor' fits should prompt review of data accuracy and caution interpreting predictions.
  - Fit of most recent levels most important and settings can be changed to use a different model or "flattened prior" (see InsightRX tip sheets in S-drive "vanco per pharm").
  - Additional TDM will be helpful if poor fit; consider getting two concentrations within the same dosing interval.
- Reassess kidney function, toxicity, and risks.

FOLLOW UP MONITORING

- The following scenarios may warrant rechecking vancomycin TDM and/or serum creatinine (SCr) within 24 hours of:
  - Change in vancomycin dose
  - 'Poor' model fit within InsightRX
  - Change in renal function/ urine output or dialysis mode
  - Addition of nephrotoxic medication, including intravenous contrast (refer to NINJA)
  - Surgical procedure or major event (e.g., ischemic event, cardiac arrest)
- Renal function (e.g., SCr, BUN, urine output) should be monitored every 24 - 48 hours until stable vancomycin dosing is achieved.
- Recheck SCr every day after 3 days of vancomycin while inpatient, per NINJA protocol.
- Frequency of monitoring should be based on clinical judgment, however monitoring of vancomycin serum concentration in stable patients should be at least once weekly.

REFERENCE

Rybak MJ, et al. Therapeutic monitoring of vancomycin for serious methicillin-resistant Staphylococcus aureus infections: A revised consensus guideline and review of 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. Clin Infect Dis. 2020 Sep 12;71(6):1361-1364.