UNC MEDICAL CENTER GUIDELINE

# Vancomycin Dosing & Monitoring Guide: Neonatal & Pediatric

This guideline is intended to provide intuitional-specific guidance on vancomycin dosing and monitoring in neonatal and pediatric patients. Specifically, this document includes guidance to assist pharmacists in identifying patients that may qualify for continuous infusion vancomycin (CIV) and provide recommendations on dosing, monitoring, and special considerations related to the administration of CIV.

## Contents



### INITIAL DOSING

Based on patient's age, actual body weight, renal function, and indication

**Table 1. Neonatal**

| Dose | PMA (weeks) | Postnatal Age (days) | Interval (hours) |
|---|---|---|---|
| 15 mg/kg/dose | ≤ 29 | 0-14<br>> 14 | 12<br>12 |
| 15 mg/kg/dose | 30-36 | 0-14<br>> 14 | 12<br>8 |
| 15 mg/kg/dose | 37-44 | 0-7<br>>7 | 12<br>8 |
| 15 mg/kg/dose | ≥ 45 | ALL | 8 |

PMA (postmenstrual age) = gestational age + weeks of life

**Table 2. Pediatric***

| Age | Empiric Regimen (IV) | |
|---|---|---|
| | Dose | Interval (hours) |
| 1 month to 3 months | 15 mg/kg/dose | 8 |
| 4 months-10 years | CIV preferred (page 3). Otherwise, 20 mg/kg/dose every 6 hours | |
| >10 years | 20 mg/kg/dose (max initial dose 2,000 mg) | 6-8 |

*Patients ≥ 1 month (corrected gestational age)

Consider renal function, clinical status, concurrent nephrotoxic agents, and previous dosing


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## RECOMMENDED TROUGH CONCENTRATIONS FOR INTERMITTENT INFUSION DOSING

| Goal Trough (mcg/mL) | Indication |
|---|---|
| 8 – 12 | Febrile neutropenia (with **negative** cultures) |
| 10 – 20 | All other indications*†<br>*(including, but not limited to, febrile neutropenia with positive cultures, urinary tract infection, skin / soft tissue infection, and sepsis rule out without hemodynamic instability, osteomyelitis[1], pneumonia)* |

*In patients who have disseminated MRSA, CNS involvement, suspected/confirmed endocarditis, or are septic and hemodynamically unstable, consider using continuous infusion vancomycin (CIV). Targeting troughs > 15 with intermittent infusions may also be considered if CIV is not an option; please read footnote below for guidance.

†There are insufficient data to confirm the need for troughs > 15 in pediatric patients receiving intermittent infusion vancomycin. Consider patient's renal function and severity of infection prior to targeting troughs >15.

[1] Skin and soft tissue infections with hardware or clinical evidence of bone involvement should be treated as presumed osteomyelitis

## THERAPEUTIC DRUG MONITORING

**Trough Monitoring**:

- Initial trough should be drawn within 60 minutes prior to the 4th dose (approximately steady state)
- Once therapeutic trough obtained, recheck every 5-7 days for patients who will remain on therapy for ≥7 days
    - Within 24 hours if renal function declines or clinical status changes
    - Obtain trough every 3-4 days in the following patients:
        - PMH/PMT or PICU patients (minimum of twice weekly recommended)
        - Patients on concomitant nephrotoxic agents (such as aminoglycosides, NSAIDs, piperacillin/tazobactam, high dose diuretics, amphotericin, etc.)
        - Patients with higher trough goals (15-20 mcg/mL)
        - Patients on high dose vancomycin (>100 mg/kg/day)
- Consider rechecking trough following surgery or other episodes of significant hemodynamic changes
- Dose adjustments and lab orders per Pharmacy to Dose policy
    - EXCEPTION: NCCC - notify team prior to placing orders for dose changes and labs
- Assess patient frequently and narrow therapy as indicated
    - Monitor renal function closely (daily urine output and serum creatinine at least weekly)
        - If there is a change in renal function, a trough should be obtained immediately prior to administration of the next dose. If extreme change in SCr or UOP, consider holding next dose of vancomycin until trough has resulted.
- Consider contacting the Pediatric Antimicrobial Stewardship Team if unclear indication or trough goal
    - Pediatric Antimicrobial Stewardship Team pager: 123-4031

**Alternative Monitoring**: In select patients, vancomycin may be adjusted to achieve AUC24 of 400-650 mg*h/L. The minimum trough concentration for patients monitored by AUC24 is 8 mg/L. Currently, this type of monitoring requires obtaining two vancomycin levels. Please see the Appendix for AUC calculations, or the Vancomycin AUC Excel PK Calculator may be used.

- Two serum concentrations should be drawn approximately 2 hours after the end of infusion, and within 60 minutes of the next dose. The provided Excel calculator will be used to adjust regimen to achieve AUC24 400-650 mg*h/L.

## CONSIDERATIONS IN RENAL IMPAIRMENT

- CrCl < 10-50 mL/min/1.73m2, hemodialysis (HD), peritoneal dialysis (PD), or continuous renal replacement therapy (CRRT)
    - Give 15-20mg/kg IV x1 dose only
    - Obtain random level 12-24 hours post vancomycin infusion
    - If level within goal (as above), re-dose and repeat level in 12-24 hours
    - If level supra-therapeutic, continue to hold and recheck level in 12-24 hours
    - While inpatient, vancomycin levels may be obtained immediately before HD or 2-3 hours after completion of a dialysis session, to allow for redistribution of fluids.
    - For HD patients receiving vancomycin outpatient, it is recommended to obtain a vancomycin level immediately prior to the HD session.
    - A full four-hour session removes ~30% of the pre-HD level.
    - Post-HD levels are not recommended in this setting as it requires the patient to wait 2-3 hours after end of a dialysis session to allow for fluid redistribution prior to obtaining the level appropriately.
    - Vancomycin levels are not required for patients receiving vancomycin via intraperitoneal route, unless there is concern for systemic exposure/toxicity or if the patient is also receiving intravenous vancomycin.

## ADJUSTMENT BASED ON TROUGH SERUM CONCENTRATIONS

- Method 1: Since vancomycin pharmacokinetics are linear, the dose may be adjusted proportionally according to the desired concentration.
- Method 2: A patient-specific $K_e$ can be calculated from a steady-state trough concentration:

$$k = \frac{-\ln\left[\frac{[\text{trough X Vd (L/kg) X wt (kg)}]}{[\text{dose (mg)}]}\right]}{1+\left(\frac{[\text{trough X Vd (L/kg) X wt (kg)}]}{[\text{dose (mg)}]}\right)}}{\text{Tau}}$$

Tau = dosing interval, $V_d$ = population $V_d$ (if no patient specific $V_d$ available)

## CONTINUOUS INFUSION VANCOMYCIN GUIDANCE

Vancomycin has become a mainstay of therapy for treatment of pneumonia, osteomyelitis, septic arthritis, endocarditis, and other infections caused by methicillin-resistant Staphylococcus aureus (MRSA). Traditionally, in order to achieve maximum efficacy, vancomycin is dosed to target trough concentrations of 10-20 mg/L depending on the site of infection. However, more recently there have been newer studies that support moving away from trough monitoring and instead recommend targeting a ratio of the area under the curve for a total daily dose ($AUC_{24}$) to minimum inhibitory concentration (MIC) of 400-650 mg h/L based on the pharmacokinetic profile of vancomycin. Often in pediatrics, trough levels remain sub-therapeutic despite aggressive dose increases or changes in frequency of doses. This failure in achieving therapeutic trough levels is almost directly attributed to the enhanced clearance of vancomycin in the pediatric population. CIV provides an advantage over intermittent dosing in certain patients because it maximizes the time-dependent activity of vancomycin by reaching targeted concentrations more rapidly with less variability in levels. Additionally, CIV also simplifies the process of serum-level monitoring for nurses/phlebotomists, often reduces the total daily dose of vancomycin required for goal steady state concentration ($C_{ss}$) and may lead to less incidences of vancomycin-associated nephrotoxicity.

## ELIBIGLE PATIENTS FOR CIV

| Inclusion | Exclusion |
|---|---|
| Central Line Access* | If only line access is via the central line and receiving other medications that are non-compatible via Y-site |
| Normal Renal Function<br>(SCr < 0.9 mg/dL or UOP ≥ 1 ml/kg/hr) | Renal Impairment<br>(Serum creatinine increase of 0.5 mg/dL or ≥ 50% increase from baseline or a decrease in creatinine clearance of 50% from baseline) |
| Patients admitted to pediatric medicine services within the University of North Carolina Children's Hospital | |

*Central line access is preferred however if clinically necessary it is acceptable to utilize a peripheral line

## CIV DOSING

Loading Dose:

- Consider a loading dose in patients who have stable renal function and have not received IV vancomycin in the last twelve hours prior to starting CIV.
- Loading dose = 15-20 mg/kg infused over one hour followed immediately by starting CIV dose.

Regardless of age, consider initiating patients with febrile neutropenia or cystic fibrosis at 60 mg/kg/day due to increased clearance

| Age Range | Initial Dose* |
|---|---|
| 1 month to < 2 years old | 60 mg/kg/day |
| 2 to < 10 years old | 50 mg/kg/day |
| 10 to < 18 years old | 40 mg/kg/day |

*Initial dose is independent of prior intermittent infusion dosing regimen

## CIV LAB MONITORING

- Target serum vancomycin concentration (SVC) of 20-25 mg/L
  - AUC = $C_{ss}$ x 24
  - SVC of 20-25 mg/L correlates with an AUC of 480-600 mg*h/L
- Obtain a level 24 hours after start of infusion and then every 24 hours thereafter until two consecutive therapeutic levels have been achieved
  - Levels may be drawn centrally with appropriate line flush per nursing policy or peripherally
  - This information is summarized in the dotphrase ".CIVLEVEL" and may be included in the level order
- Once 2 consecutive therapeutic SVCs are obtained, can space out monitoring to every 5-7 days as long as renal function is stable
- Estimated new dosing rate = current daily dose x desired $C_{ss}$ / measured $C_{ss}$

| Serum Vancomycin Concentration (mg/L) | Dose Adjustment |
|---|---|
| < 20 | Titrate by 10-15% of total daily dose to achieve goal $C_{ss}$ |
| 20-25 | Continue with current regimen |
| 26-30 | Consider empiric dose reduction by 10-15% of total daily dose to achieve goal $C_{ss}$ |
| > 30 | Hold infusion for 4 hours, recheck level, and then resume infusion rate at a lower total daily dose |
| > 40 | Hold infusion for 12 hours, recheck level, and then resume infusion rate at a lower total daily |

**CIV SPECIAL CONSIDERATIONS**

- Monitor for signs of phlebitis or infusion related reaction
    - Can administer diphenhydramine and/or famotidine if clinically indicated
- **Incompatible (Y-site) medications include*:** potassium phosphate, heparin, piperacillin/tazobactam, hydrocortisone, ceftazidime, furosemide, methylprednisolone and phenytoin
- **Compatible (Y-site) medications include*:** aminoglycosides, ciprofloxacin/levofloxacin, fluconazole, insulin and morphine
- **Avoid concomitant use of nephrotoxins including*:** acyclovir, aminoglycosides, amphotericin, calcineurin inhibitors, furosemide, NSAIDs, and vasopressors

*Not a comprehensive list, for additional medication considerations refer to tertiary drug resources

**REFERENCES**


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