Vancomycin IV Therapeutic Drug Monitoring (Adults)

Vancomycin, a glycopeptide antibiotic used for the treatment of infections caused by gram-positive organisms, can lead to serious toxicity and adverse events. Dosing and monitoring of IV vancomycin is important for patient safety and treatment efficacy, and should be done with clinical pharmacy support.

Area-under-the-curve (AUC) guided strategy for IV vancomycin dosing is recommended for all adult patients on therapeutic IV vancomycin, with a target AUC_{24h}/MIC of 400-600. AUC_{24h}/MIC above 600 is associated with increased risk of renal injury.

Patients who are critically ill and/or with a central nervous system (CNS) infection should be dosed at the higher end of the proposed AUC_{24h}/MIC range (i.e. 500-600).

The following recommendations and calculation tools should not apply for:

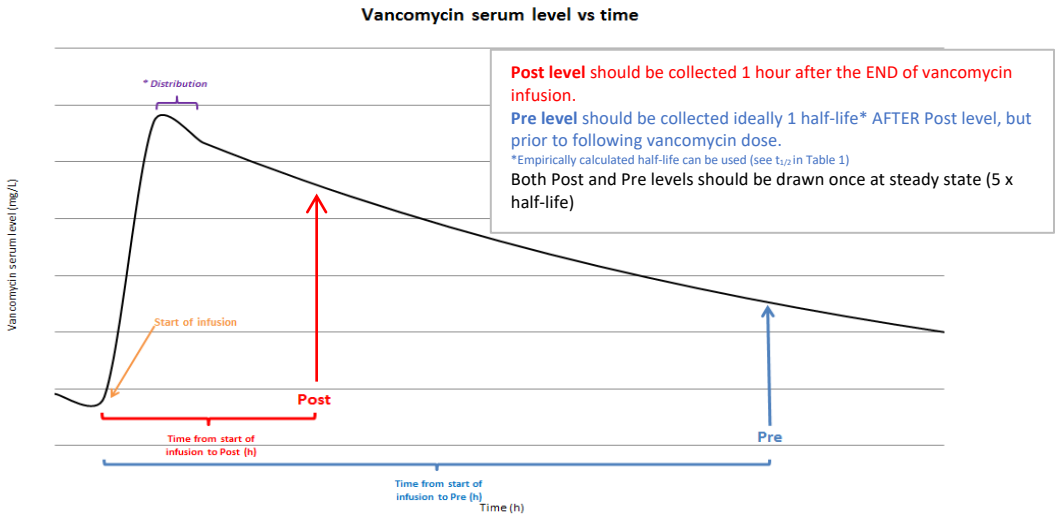
- *Patients in AKI (single doses should be determined on a daily basis with pharmacy support)*
  - *Definition of AKI (RIFLE criteria): 1.5x serum creatinine above baseline, > 25% decrease in GFR and/or < 0.5 mL/kg/hour for 6 hours*
- *Patients on renal replacement modality (IHD, PD or CRRT) (Dosing should be determined with nephrology and/or pharmacy support)*

INITIAL EMPIRIC DOSING

1. The initial dosing regimen should be based on populational pharmacokinetic parameters.
   **Please refer to "Initial Dosing" section on https://vanco.medsafer.org/*
2. A **loading dose** should be given to patients with hemodynamic instability, CNS infection, MRSA bacteremia, febrile neutropenia, necrotizing fasciitis and CKD.
   **Please refer to "Initial Dosing" section on https://vanco.medsafer.org/*

MONITORING AND ADJUSTMENT

1. Once renal function and volume status are stable and vancomycin is at steady state*, **draw a set of 2 serum vancomycin levels** after a specified vancomycin infusion and prior to next vancomycin dose to determine AUC_{24h}/MIC *(Post and pre levels without dose in between levels)*.



Set of vancomycin levels should be drawn to determine AUC_{24h}/MIC only in patients who will **continue IV vancomycin <u>for more than 48 hours</u>.**
If AUC_{24h}/MIC is not within target, adjust dosing regimen to achieve target**.
If AUC_{24h}/MIC is within target, continue same dosing regimen.

** Vancomycin steady state is achieved once patient has been receiving vancomycin at a designated dosing regimen without interruption for the duration of <u>5 half-lives</u>*
(Please refer to Box C in "Initial Dosing" section on https://vanco.medsafer.org/ for populational estimate of half-life)

*** Please refer to "Dose adjustment – 2 level" section on https://vanco.medsafer.org/*

If there is any significant change in renal function and/or volume status, reassess dosing with repeat "set of vancomycin levels" once renal function and volume status have stabilized.

2. Otherwise, draw a vancomycin trough level:
    - After initiation or adjustment of dose, to confirm that predicted trough is achieved (within 25% of expected value)
    - At least once weekly while on IV vancomycin therapy, to confirm that trough is still within target (trough within 25% of previous values)

3. Serum creatinine and CBC weekly

OUTPATIENT PARENTAL ANTIMICROBIAL THERAPY (OPAT)

AUC monitoring is not feasible in an OPAT context. Therefore, an AUC dosing strategy and monitoring is <u>not recommended for OPAT.</u> We suggest instead that prior to discharge, a target trough range be determined by ID/pharmacy to guide IV vancomycin dosing. Patients should be clinically stable (stable renal function and volume status) when determining this range.

ADDITIONAL COMMENTS

- AUC dosing strategies are associated with lower risk of nephrotoxicity when compared to trough dosing strategies targeting over 15 mg/L. Please note that <u>there has not been any head-to-head studies comparing AUC dosing strategies with trough dosing strategies with lower target range (5-15 mg/L).</u>
- The evidence supporting a AUC_{24h}/MIC target of 400-600 is **mainly derived from MRSA infections.** It is still unclear what the optimal targets and dosing strategies for IV vancomycin are for infections with other organisms (*Enterococcus sp*, coagulase-negative staphylococci [CoNS], MSSA, etc.)
- In cases where MRSA MIC is lower than 1 mg/L, target for absolute AUC_{24h} should still be over 400. In most cases the MIC will not be specifically determined and will be **assumed to be 1 mg/L.**
- Indication for IV vancomycin therapy should be regularly assessed as risk of nephrotoxicity depends on duration of therapy, target levels and concomitant use of other nephrotoxic agents.

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