

## ADULT INTRAVENOUS VANCOMYCIN DOSING AND MONITORING GUIDELINES

**DOSE:** Adult dose: (based on actual body weight (ABW))\*^:

**12.5 to 15 mg/kg** (round off to nearest 250 mg increment, to max dose of 1500mg; see dosing table)

\* If ABW is > 30% ideal body weight (IBW), then use adjusted body weight = IBW + 0.4(Total body weight - IBW)

IBW Males = 50 kg + 2.3 kg for each inch > 60 inches      IBW Females = 45 kg + 2.3 kg for each inch > 60 inches

^ Give a *Loading Dose* of 20mg/kg IV x 1 (1<sup>st</sup> dose) for severe sepsis/shock and/or suspected or confirmed deep-seated infections.

<u>VANCOMYCIN DOSES</u>		
<u>Traditional Dosing:</u> goal trough 10-15 mcg/mL		<u>High Dosing:</u> goal trough 15-20 mcg/mL
Weight (kg)	Maintenance Dose ~ 12.5 to 15mg/kg / dose	Maintenance Dose ~ 15mg/kg / dose
> 90	1250	1500
76-90	1000	1250
55-75	1000	1000
45- 55	750	750

- Contact your service pharmacist for information on morbidly obese or markedly fluid-overloaded patients

### INTERVAL:

<u>VANCOMYCIN DOSING INTERVAL BASED ON ESTIMATED CrCL*</u>			
<u>Traditional dosing:</u> Goal Tr = 10-15 mcg/ml		<u>High Dosing:</u> Goal Tr = 15-20 mcg/ml	
CrCL (ml/min)	Dosing Interval (hrs)	CrCL (ml/min)	Dosing Interval (hrs)
> 65	q12h	> 100	q8h
30-65	q24h	66-100	q12h
< 30 or dialysis	contact pharmacist	30-65	q24h
		< 30 or dialysis	contact pharmacist^

\* CrCL = Creatinine Clearance (Calculation): use minimum SCr of 1mg/dl in elderly and cachectic patients; Tr = trough

^ Dosing recommendations in hemodialysis are presented on the next page

**Need to reduce total daily dose for debilitated or elderly patients - no more frequent than q24h dosing for >79yrs**

### MONITORING:

Usually only vancomycin troughs are needed. Random levels may be obtained on patients with poor renal function who only receive intermittent or post-dialysis dosing. At minimum, levels should be obtained for all patients by 72 hours of therapy and at least weekly thereafter. Many patients will require more frequent monitoring. Chemistries and CBCs should also be checked at least weekly. Monitoring in hemodialysis is presented on the next page.

#### Early serum level testing to ensure adequate dosing:

- Central nervous system infections
- *S. aureus* sepsis w/ clinical instability
- Osteomyelitis
- Ventilator associated & hospital-acquired pneumonia
- Endocarditis
- Persistently positive gram-positive bacteremia

#### Conditions requiring early and more frequent lab testing:

- Rapidly changing renal function
- Poor renal function or on dialysis
- Co-administration with nephrotoxic drugs
- Target trough level of 15 – 20mcg/ml
- For information on appropriate use of levels in dialysis, please see next page; call your service-based pharmacist

The service pharmacist can assist with questions regarding vancomycin dosing, monitoring or level interpretation.

#### When to draw levels:

Trough: just before 4th dose of a new regimen (prior to 3<sup>rd</sup> dose for dosing intervals ≥ 24 hours or changing renal function)

- Trough levels should be obtained within 30 minutes before the next scheduled dose.
- Weekly vancomycin levels should be obtained for long-term vancomycin use with stable renal function.

#### Desired Levels:

Traditional dosing: 10-15 mcg/ml (to achieve concentration ≥ 4 x MIC of directed pathogen at the site of infection)

High dosing: 15-20 mcg/ml (deep-seated gram-positive infections, CNS infections, or as recommended by ID)

**\*\*\* Caution\*\*\* Troughs > 15mcg/ml have been associated with higher rates of nephrotoxicity**

## Vancomycin Continuous Infusion (CI)

### A. Background

1. May be renal protective compared to troughs of 15-20mcg/ml via intermittent dosing
2. Effective method to achieve adequate levels in pts with high elimination rates (i.e.  $Cl_{Cr} > 120$  ml/min, e.g. burn, TBI, severe trauma)
3. Review need for continued vancomycin therapy (for 4 days or more)
4. Confirm central venous access and medication compatibility with RN (Lexicomp, Micromedex)
5. Define therapeutic targets ( $AUC \rightarrow C_{ss}$ ) based on indication and MIC, call ID pharm for help
6. Contact ID pharmacist if planned extended duration or ID Service consulting

<u>Indications</u>	<u>Targets</u>	
	AUC (mg·hr/L)	$C_{ss}$ (mg/L)
<b>Deep-seated infection</b> (e.g. PNA, endocarditis, CNS infection, deep abscess)  <b><i>Staphylococcus aureus</i> bacteremia</b>  <b>Severe infection</b> (e.g. severe sepsis, septic shock, TSS, PCT > 5 ng/ml)	<b>400 – 530</b>	<b>17 – 22</b>
<b>UTI, skin &amp; soft tissue infections, MIC <math>\leq</math> 0.5</b>	<b>240 – 360</b>	<b>10 – 15</b>

TSS = toxic shock syndrome; PCT = procalcitonin

- a)  $AUC_{CI}$  (mg·hr/L) = concentration (mg/L) x 24 hrs
- b) Example:  $AUC = (17 \text{ mg/L}) \times (24 \text{ hrs}) = 408 \text{ mg·hr/L}$

7. Evaluate renal function and calculate  $Cl_{Cr}$ , anticipating potential changes in renal function

### B. Converting intermittent to continuous dosing

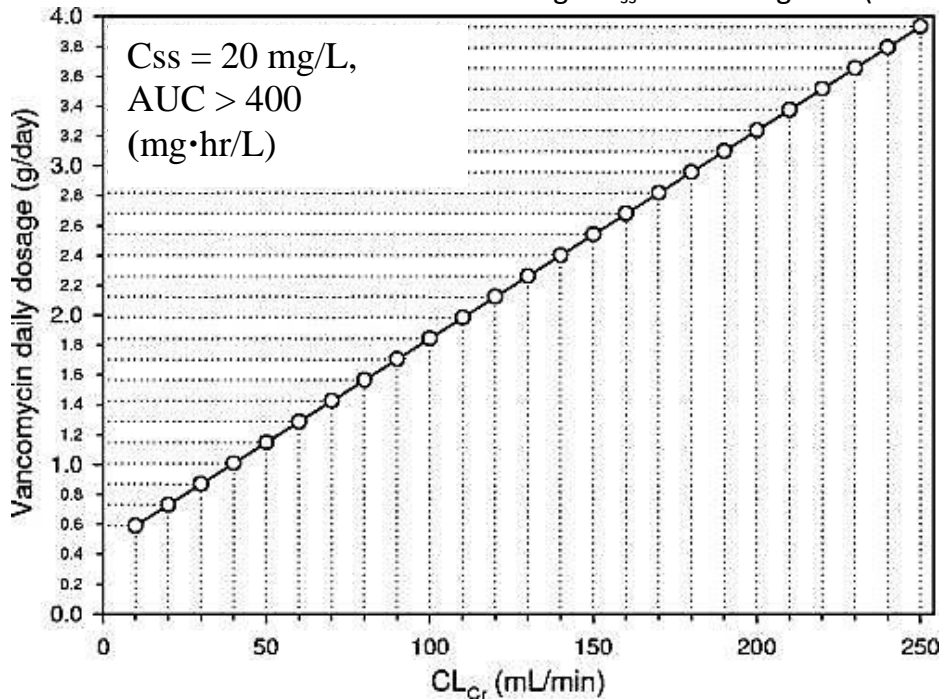
1. Steady state, target trough within target range
  - a) Continuous infusion (mg/day) = (total daily dose, intermittent) x (0.6)
  - b) Double-check dose with nomogram (below)
  - c) Start continuous within 1 hour of next/last intermittent dose
2. Steady state level is sub- or supra-therapeutic
  - a) Calculate “new dose” for intermittent dosing
    - i. 
$$\text{new dose (mg/day)} = \frac{(\text{target level})}{(\text{measured level})} \times \text{current dose (mg/day)}$$
  - b) Continuous infusion (mg/day) = (“new dose,” via intermittent) x (0.6)
  - c) Start continuous within 1 hour of next/last intermittent dose
3. Not at steady state OR no levels available
  - a) Calculate  $Cl_{Cr}$  using IBW, adjust prn for patient-specific factors
  - b) Use nomogram(s) below
  - c) Start continuous within 1 hour of next/last intermittent dose

### C. Vancomycin new start

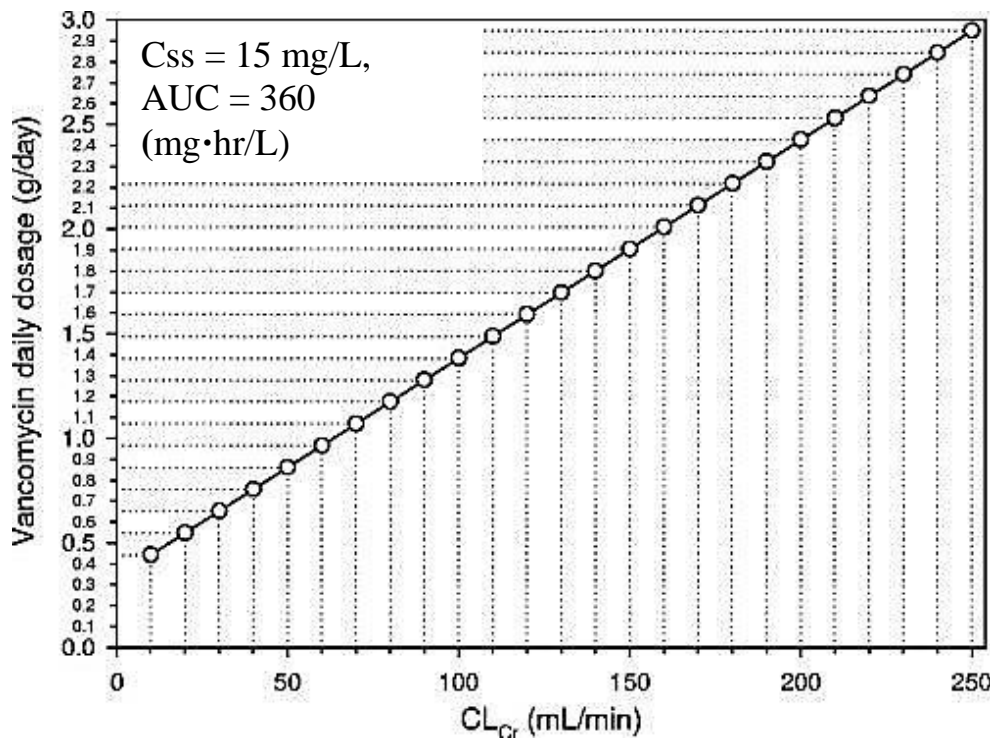
1. Calculate loading dose for patients NOT already on vancomycin

<u>Clinical Scenario</u>	<u>Suggested load</u>	<u><math>C_{peak}</math></u>
<b>critically ill</b>		
$Cr_{Cl} > 30$ ml/min	25 mg/kg	35 mg/L
$Cl_{Cr} < 30$ ml/min	20 mg/kg	28 mg/L
<b>mild – moderate infection</b>		
$Cr_{Cl} > 30$ ml/min	20	28 mg/L
$Cl_{Cr} < 30$ ml/min	15	20 mg/L

2. Select maintenance dose based on target  $C_{ss}$  and nomograms (below)



Indications:  
 PNA,  
 endocarditis,  
 CNS infection,  
 deep abscess



Indications:  
 UTI, skin & soft  
 tissue infections,  
 peritonitis,  
 MIC  
 $\leq 0.5 \text{ mcg/ml}$

**D. Logistics (EMR)**

1. **Patients NOT previously receiving vancomycin** → order load + continuous infusion
  - a) Select "Vancomycin IV"
  - b) Order loading dose based on calculation (above) and change frequency to "ONCE"
  - c) **Communication:** add administration instructions- "LOADING DOSE. Please start continuous infusion immediately after loading dose."
2. **Patients on intermittent dosing strategy**, change order so that it expires after next dose
  - d) Modify order, select "Change End Time" to "End after" 1 more dose
  - e) Communication: **relay plan to RN**, document in Ivent

3. Order continuous infusion
  - f) Select “Vancomycin IV Continuous Infusion” in order entry
  - g) Standard concentration is 2 grams in 500ml NS
  - h) Make sure the label notes this is a CONTINUOUS INFUSION and the RN instructions state to run through central line
4. Verify orders
  - i) Continuous infusion
    - i. Ensure infusion rate is correct
    - ii. Re-time continuous infusion to start immediately after loading dose
    - iii. With dose adjustment use “modify” function, not DC and reorder

## E. Monitoring

1. “random levels”:  $C_{min} = C_{peak} = C_{random}$

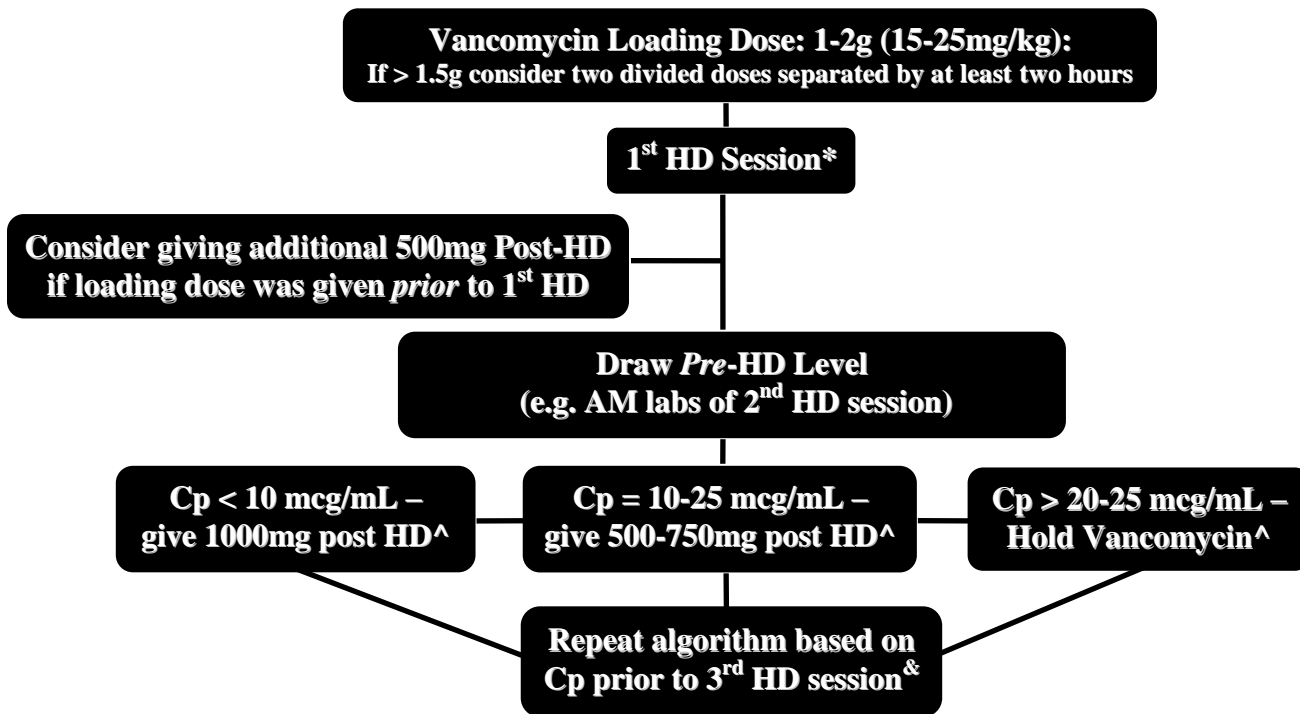
<b>Estimated renal function (<math>Cl_{Cr}</math>)</b>	<b><math>t_{1/2}</math> (hrs)</b>	<b>steady state (hrs)</b>
> 120 ml/min	4 – 6	12 – 24
90 – 120 ml/min	8	24 – 36
60 – 90 ml/min	12	36 – 48
30 – 60 ml/min	24	72 – 96
15 – 30 ml/min	48	144 – 288*
< 15 ml/min	72 – 96+	(1 – 2 wks)

2. Order random vancomycin level within 24 – 36 hours of initiation (with AM labs best)
  - a) Repeat QAM until level stays within 10-15% variation from previous
  - b) After any dose adjustment, repeat level within 24 – 48 hours or at estimated steady state
  - c) Repeat random levels every 3 – 7 days depending on renal function changes or toxicity risk
3. Dose adjustment
  - a)  $new\ dose\ (mg/day) = \frac{(target\ level)}{(measured\ level)} \times current\ dose\ (mg/day)$
  - b) Example: measured level = 12 mg/L, target = 17 mg/L, current dose = 1,750 mg/day
    - i.  $new\ dose\ (mg/day) = \frac{(17\ mg/L)}{(12\ mg/L)} \times 1,750\ mg/day = 2,500\ mg/day$
  - c) Example: measured level = 20 mg/L, target = 17 mg/L, current dose = 1,750 mg/day
    - ii.  $new\ dose\ (mg/day) = \frac{(17\ mg/L)}{(20\ mg/L)} \times 1,750\ mg/day \approx 1,500\ mg/day$

## F. Communication

1. Nurse:
  - a) Alert RN to start continuous infusion **IMMEDIATELY** after completion of loading dose or next/last dose intermittent dose
  - b) Clarify y-site compatibility: consider providing print out from Lexicomp or Micromedex
  - c) Double-check admin instructions: Run through central line, Please contact Pharmacy (3-4072) if central venous access is compromised
  - d) Vancomycin continuous infusions do NOT automatically appear in the continuous infusion section of flowsheets. The order appears in the “Scheduled” section of the MAR AND may be manually added to the continuous infusion flowsheet. It will appear on ID flowsheet
  - e) Instruct RN to draw levels via peripheral stick, but if from catheter (either lumen), stop vancomycin infusion for 30 seconds and flush well before drawing level
2. Pharmacist:
  - a) Ivent elements: indication,  $Cl_{Cr}$ , target  $C_{ss}$ , pending levels, suggested monitoring
  - b) Progress note using .phrase to communicate daily dose and targeted random level

**Vancomycin Dosing in Intermittent Hemodialysis (IHD, HD)<sup>1-7</sup>**



\* Assumes one hemodialysis session removes 30-50% of vancomycin with utilization of high-flux dialysis filters.<sup>5-7</sup>

^ Redosing is dependent on reported & targeted vancomycin concentrations, use of high- vs. low-flux filters, site/severity of infection & other factors (e.g. for deep-seated gram-positive infections consider larger doses and/or higher Cp tolerance for redosing).

See tables below.

**Routine vancomycin levels prior to each dialysis session are NOT necessary in most cases and strongly discouraged. Patients receiving a stable thrice weekly dialysis regimen (e.g. MoWeFr or TuThSa) and have met target pre-HD levels on two consecutive sessions (e.g. prior to 2<sup>nd</sup> & 3<sup>rd</sup> HD sessions) can drop to once weekly levels. Most patients require 500-750mg IV post dialysis thrice weekly. Continued weekly pre-HD levels are recommended for long term courses.**

**Goal pre-HD vancomycin level = 10-20 mcg/mL (e.g. mild-moderate infections) (pts >60kg)**

Vancomycin plasma concentration	Vancomycin Dosing Recommendations (Give After Dialysis)	
	Pre-HD Level (preferred)	Post-HD Level
Cp < 10 mcg/mL	Give 1000mg IV post dialysis	Give 750-1000mg IV post dialysis
Cp 10-15 mcg/mL	Give 500-750mg IV post dialysis	Give 500mg IV post dialysis
Cp 15-20 mcg/mL	Give 500mg IV post dialysis	Hold vancomycin
Cp > 20 mcg/mL	Hold vancomycin	Hold vancomycin

**Goal post-HD vancomycin level = 15-25 mcg/mL (e.g. severe and/or deep-seated infections)**

Vancomycin plasma concentration	Vancomycin Dosing Recommendations (Give After Dialysis)	
	Pre-HD Level (preferred)	Post-HD Level
Cp < 10 mcg/mL	Give 1000-1500mg IV post dialysis	Give 1000mg IV post dialysis
Cp 10-15 mcg/mL	Give 750-1000mg IV post dialysis	Give 500-750mg IV post dialysis
Cp 15-20 mcg/mL	Give 500-750mg IV post dialysis	Give 500mg IV post dialysis
Cp 20-25 mcg/mL	Give 500mg IV post dialysis	Hold vancomycin
Cp > 25 mcg/mL	Hold vancomycin	Hold vancomycin

More aggressive dosing may be required for extended daily dialysis (EDD). Consult Pharmacy.

Please see “Antimicrobial Dosing for Renal Replacement Therapy Guidelines” for vancomycin dosing in continuous renal replacement therapy (CRRT: CVVH, CVVHD, CVVHDF).

**References:**

- 1) Rybak MJ, Lomaestro BM, Rotschafer JC, et al. Therapeutic monitoring of vancomycin in adults summary of consensus recommendations from the American Society of health-system pharmacists, the IDSA, and the society of infectious diseases pharmacists. *Pharmacotherapy*. 2009 Nov;29(11):1275-9.
- 2) Heintz BH, Matzke GR, Dager WE. Antimicrobial Dosing Concepts and Recommendations for Critically Ill Adult Patients Receiving Continuous Renal Replacement Therapy or Intermittent Hemodialysis. 2009; *Pharmacotherapy*; 29(5): 562-577.
- 3) Pallotta KE, Manley HJ. Vancomycin use in patients requiring hemodialysis: a literature review. *Semin Dial* 2008; 21:63-70.
- 4) Launay-Vacher V, Izzedine H, Mercadal L, Deray G. Clinical review: use of vancomycin in haemodialysis patients. *Crit Care* 2002; 6:313-6.
- 5) Klansuwan N, Ratanajamit C, Kasiwong S, Wangsiripaisan A. Clearance of vancomycin during high-efficiency hemodialysis. *J Med Assoc Thai* 2006; 89:986-91.
- 6) Ariano RE, Fine A, Sitar DS, Rexrode S, Zelenitsky SA. Adequacy of a vancomycin dosing regimen in patients receiving high-flux hemodialysis. *Am J Kidney Dis* 2005; 46:681-7.
- 7) Pai AB, Pai MP. Vancomycin dosing in high flux hemodialysis: a limited-sampling algorithm. *Am J Health Syst Pharm* 2004; 61:1812-6.

Approved by UCDH Pharmacy and Therapeutics Committee 12/2017.