Team Name: Pharmacy and Therapeutics Team Lead: Regional Director -Pharmacy Approved by: V P – Medical Services	Reference Number: CLI.6010.SG.001 Program Area: Pharmacy and Therapeutics Policy Section: General
Issue Date: November 26 2015 Review Date: March 13 2019 Revision Date:	Subject: Adult Vancomycin Monitoring and Dosing

STANDARD GUIDELINE:

Adult Vancomycin Monitoring and Dosing

PURPOSE:

To provide recommendations for monitoring and dosing of vancomycin. These recommendations provide guidance and the health care professional may use their judgement in patient-specific scenarios if deemed clinically appropriate.

BOARD POLICY REFERENCE:

Executive Limitation (EL-2) Treatment of Clients

IMPORTANT POINTS TO CONSIDER:

Routine monitoring of vancomycin levels is NOT recommended because there is:

- Little literature evidence to support it
- No clear evidence that nephrotoxicity and ototoxcity associated with vancomycin are prevented by adherence to specific concentration ranges

Peak (post) levels are NOT needed because:

- Vancomycin exhibits time dependent killing as opposed to concentration dependent killing (i.e. aminoglycosides); vancomycin distributes slowly into peripheral tissues, making it difficult to identify the true peak.
- They have not been correlated with improvements in clinical outcome

PROCEDURE:

Step 1 – Recommended Initial Dose and Dosing Interval:

a. Dose

- 1 gram Q12H or 15 to 20 mg/kg per dose (based on actual body weight) to a maximum of 2.5 grams per dose
- Doses greater than 500 mg – round off to the nearest 250 mg
- Doses less than 500 mg – round off to the nearest 50 mg

b. Dosing interval dertermination (Lexicomp)
   - Determine creatinine clearance (Clcr)

Clcr (male) = $\frac{(140 - \text{age}) \times \text{IBW}^{*} \times 1.23}{\text{Scr (umol/L)}}$ Clcr (female) = 0.85 x Clcr (male)

*Ideal Body Weight (IBW) (females) = 45.5 kg + [2.3 x (inches greater than 5 feet)]
IBW (males) = 50 kg + [2.3 x (inches greater than 5 feet)]

CrCl (mL/min)	Dosing regimen
Greater than or equal to 80	Q12H**
50 to 79	Q24H
35 to 49	Q36H
25 to 34	Q48H
Less than 25	Q 2 to 7 DAYS (consult pharmacist)

** consider Q8H if treating CNS infections, osteomyelitis, endocarditis or pneumonia or if patient is obese

c. Administration
   - Maximum rate of infusion: 15 mg/minute to minimize thrombophlebitis and red man syndrome
   - less or equal to 1 gram – infuse over 60 minutes
   - 1.25 gram to 1.5 grams – infuse over 90 minutes
   - 1.75 grams to 2 grams – infuse over 120 minutes
   - 2.25 grams to 2.5 grams – infuse over 180 minutes

d. Concentration
   - Maximum concentration 5 mg/mL to minimize infusion related side effects such as thrombophlebitis and red man syndrome
   - Less than or equal to 500 mg in 100 mL
   - Greater than 500 mg to 1.25 grams in 250 mL
   - 1.5 grams to 2.5 grams in 500 mL

e. Dosing recommendations for obese patients
   - The formal definition of obesity is defined as a Body Mass Index (BMI) of 30 or more. To facilitate weight-based drug dosing (not BMI), the following method is used to calculate the IBW.
     - Actual body weight is recommended when dosing obese patients. The usual maximum dose is 2.5 grams per dose.
     - A pre-level is recommended when a patient is 125% or more greater than the IBW. These patients may have altered kinetic parameters and require Q8H dosing to ensure that an adequate pre-level is achieved.

f. Loading dose
   - Generally, there is no advantage of giving a loading dose as vacomycin kills bacteria in a time-dependent manner vs the concentration-dependent manner of aminoglycosides or fluoroquinolones.
   - Exceptions: Give a loading dose of 25 mg/kg in the following patients:

- Chronic renal failure patients have significantly larger average volumes of distribution; continue empiric dosing as follows – 40 to 69.9 kg give 1 gram load then 500 mg in the last hour of each dialysis, 70 to 100.9 kg give 1.25 gram load then 750 mg in last hour of each dialysis, 101 to 130 kg give 1.5 gram load then 1 gram in last hour of each dialysis.
- Continuous ambulatory or cycling peritoneal dialysis – repeat the loading dose of 25 mg/kg every 5 days for 2 to 3 weeks therapy.
- Patients with serious MRSA infections (i.e. endocarditis, septic) – may consider a loading dose, although this is not currently supported by large randomized clinical trials.

Step 2 – Order Appropriate Laboratory Tests

(*a pharmacist can order vancomycin levels for monitoring including creatinine levels and the pharmacist must be responsible for the dosing adjustments hereafter*)

g. Serum creatinine levels

- A baseline level should be ordered
- Once weekly (more frequently if renal function changing or if concurrent nephrotoxic drugs)
- If creatinine changes, refer to adult dosing interval chart (step 1) for appropriate adjustment

h. Vancomycin serum trough levels

- Order ONLY if patient meets the criteria
- Inclusion Criteria for Vancomycin Trough Serum Level Monitoring
  - Deteriorating/unstable renal function
  - Morbidly obese patients (greater or equal to 125% IBW) – measure trough before 2nd dose to avoid overestimation and to ensure steady state trough level is likely to be therapeutic. Repeat trough level prior to 4th dose. NOTE: the pre 2nd dose trough will not be useful if vancomycin levels are tested off site as results will not be back in time to be clinically relevant.
  - Patients with anticipated therapy greater than 7 days
  - Elderly
  - Cerebrospinal fluid shunt infections, meningitis
  - Patients with rapid clearance of drug (i.e. cystic fibrosis, burns greater than 20% Body Surface Area (BSA))
  - Selected dialysis patients (i.e. high flux and continuous hemodialysis/filtration)
- To ensure steady state has been achieved, draw a trough level less than or equal to 30 minutes prior to 4th dose (e.g. after the 3rd dose), unless otherwise indicated.
- NOTE: Peak (post) levels are NOT NECESSARY (see Important Points to Consider)

Step 3 – Interpret Vancomycin Serum Trough Level

- Desired trough levels for vancomycin are approximately 10 to 20 mg/L

NOTE: Previous literature suggested trough concentrations of 5 to 10 mg/L were desirable for optimal therapeutic response, however, recent evidence suggests trough levels should always be maintained above 10 mg/L to avoid the development of resistance.

- However, there are desired trough levels for specific clinical indications
- Conditions requiring pre-levels 15 to 20 mg/L
  - Catheter-associated bacteremia
  - CNS infection
  - Deep-seated or sequestered infection (i.e. abscess)
  - Endocarditis (except for prosthetic valve endocarditis caused by Staphylococci)
  - Osteomyelitis
  - MRSA bacteremia, pneumonia, or skin and soft tissue infection
  - MSSA bacteremia (penicillin allergic patient)

i. Dosing adjustments for target trough levels of 15 to 20 mg/L:

Measured trough (mg/L)	Dosing interval adjustment	OR Dose adjustment
Less than 15 mg/L and interval greater than Q12H	*Decrease interval* by 12 hours increment	None
Less than 15 mg/L and on Q12H	*Decrease interval* to Q8H, or consider alternative therapy if possible	Increase dose by 250 mg to 500 mg at the same time interval (Q12H)
15 to 20 mg/L	No change (desired level)	No change (desired level)
Greater than 20 mg/L	*Increase interval* by 12 hours increment, OR consider alternate therapy if possible	Decrease dose by 250 mg to 500 mg at the same time interval

- Conditions requiring pre-levels approximately 10 to 15 mg/L
  - Skin and soft tissue infection not due to MRSA
  - Urinary tract infection (catheter-associated, rule out bacteremia)

j. Dosing adjustment for target trough levels of 10 to 15 mg/L:

Measured trough (mg/L)	Dosing interval adjustment	OR Dose adjustment
Less than 10 mg/L and interval greater than Q12H	*Decrease interval* by 12 hours increment	None
Less than 10 mg/L and on Q12H	*Decrease interval* to Q8H, or consider alternative therapy if possible	Increase dose by 250 mg to 500 mg at the same time interval (Q12H)
10 to 15 mg/L	No change (desired level)	No change (desired level)
Greater than 15 mg/L	*Increase interval* by 12 hours increment, OR consider alternate therapy if possible	Decrease dose by 250 to 500 mg at the same time interval

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