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Empiric Vancomycin Dosing

Dosing

- Doses calculations should be based on actual body weight and rounded to the nearest 250 mg.
- Loading doses should be considered in the setting of critical illness, severe/complicated MRSA infections (i.e. osteomyelitis, meningitis, endocarditis), or intermittent dialysis where rapid attainment of target trough is clinically warranted.

	Loading Dose	Maintenance	Frequency
Standard	20 - 35 mg/kg	15 mg/kg	See 'Frequency' below
Modified (Obesity)	20 – 25 mg/kg	15 mg/kg	See 'Frequency' below

Recommended maximum loading dose of 3 g; Recommended maximum total daily dose of 4 g

Frequency

- Recommendations for dosing frequency are based on patients with stable renal function.
- Dosing strategies should be selected based on desired trough target, taking into account infection severity and the patient's clinical status (see Initiating Vancomycin TDM).
- When selecting frequency, consider states where the estimated creatinine clearance may be an overestimate (e.g. Low muscle mass in elderly patient, neuromuscular disease, paraplegia, etc.).

Trough Target of 10 - 15 mg/L

If renal clearance calculation is available and reliable

CrCl (mL/min) or eGFR (mL/min/1.73m²)	Initial Dosing Frequency	
60 or greater	q12hr	
30 – 59	q24hr	
Less than 30	Consider Intermittent Dosing with TDM	

If renal function is not available or reliable

	Age (years)				
SCr (micromol/L)	Below 40	40-49	50-59	60-69	70 and Older
40-60			a12hr	q12hr	
61-80	a12hr	q12hr	q12hr	q24hr	q24hr
81-100	q12hr		a24br		
101-120		q24hr	q24hr		
121-140	q12-24hr				
Above 140	Consider Intermittent Dosing with TDM				

Trough Target of 15 - 20 mg/L

			Age (years)		
SCr (micromol/L)	Below 40	40-49	50-59	60-69	70 and Older
40-60	aOhr	q8hr	q8hr	q8-12hr	a12br
61-80	q8hr	q8-12hr	a12br	q12hr	q12hr
81-100	~1.2h.	q12hr	q12hr		
101-120	q12hr	q12-24hr (q12-24hr	q12-24hr
121-140	. 42 24		q12-24hr		
141-160	q12-24hr				
161-180	q24hr	q24hr	q24hr		
Above 180	Above 180 Consider Intermittent Dosing with TDM				



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Initiating Vancomycin Therapeutic Drug Monitoring (TDM)

Criteria for Vancomycin TDM

Vancomycin monitoring should only be initiated after it is confirmed that ongoing therapy is needed. Patients with short (48 hours or less) empiric courses of vancomycin do not require routine TDM.

Vancomycin monitoring should be considered for the following patients:

- Obesity
- Patients with unstable renal function or receiving dialysis
- Severe or critical illness (i.e. sepsis)
- Patients with target troughs of 15 20 mg/L
- Vancomycin treatment is expected to be 7 days or greater
- Patients at increased risk of nephrotoxicity (e.g. use of concomitant nephrotoxic agents)

Determining Target Trough Level

Trough target levels of 10 – 15 mg/L are appropriate for most infections where vancomycin is indicated. These include skin and soft tissue infections, urinary tract infections, and non-*S.aureus* associated bacteremias without a deep-seated source.

Trough target levels of 15 – 20 mg/L can be considered in patients with severe sepsis, endocarditis, infections involving the central nervous system, bone & joint infections, and serious infections involving methicillin-resistant *S. aureus* (e.g. bacteremia, pneumonia).

Initial Trough Monitoring

- Serum trough levels should be obtained 30 minutes or less prior to scheduled dose.
- In patients with stable renal function, initial trough levels should be obtained at steady state. As a general guide, the following times for serum levels are suggested:
 - o **Q8HR** frequency obtain level pre-5th dose
 - o **Q12HR** frequency obtain level pre-4th dose
 - Q24HR frequency obtain level pre-3rd or pre-4th dose depending on clinical context[†]
 - [†] In patients with reduced renal clearance, steady state may be achieved beyond 48 hours from initiation; trough levels may be required earlier than pre-4th interval (within initial 48 hours) to assess for safety.
- In patients with unstable or fluctuating renal function, it may be appropriate to obtain trough levels prior to steady state depending on clinical context. Clinical judgement, consideration of patient's status and severity of infection should guide decision of trough timing.
- For patients undergoing renal replacement therapy, see Vancomycin TDM in Dialysis

Ongoing Trough Monitoring

- Trough levels should be interpreted with consideration to changes in renal function, administration time of preceding vancomycin dose, and recent changes in vancomycin dose.
- When ongoing vancomycin TDM is indicated, trough levels should be obtained once weekly.
- If the vancomycin regimen is changed in a patient with stable renal function, trough levels should be taken at steady state of the **new** regimen (see steady state guide above).
- Renal function (i.e. SCr) should be monitored no less than once weekly. More frequent monitoring
 is recommended in patients with unstable or changing renal function, and in patients on
 concomitant nephrotoxic drugs.



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Vancomycin TDM in Dialysis

Dosing

- Doses should be rounded to the nearest 250 mg increment
- Dose calculations should be based on actual body weight
- Loading doses should be considered in the setting of critical illness, severe/complicated MRSA infections (i.e. osteomyelitis, meningitis, endocarditis), or intermittent dialysis where rapid attainment of target trough is clinically warranted.

Hemodialysis

Weight	Loading Dose	Maintenance	Frequency
Less than 70 kg	1,000 mg	500 mg	
70 – 100 kg	1,250 mg	750 mg	qHD
Greater than 100 kg	1,500 mg	1,000 mg	

Trough Level Monitoring

- Serum trough levels should be obtained 30 minutes or less prior to the next dialysis session.
- Pre-dialysis trough levels are preferred; however, if a post-dialysis level is merited, post-dialysis trough levels should be obtained at least 2 hours after the end of the dialysis session.
- Trough levels should be interpreted with consideration to changes in renal function, dialysis timing, administration time of preceding vancomycin dose, or changes in vancomycin dose.
- When ongoing vancomycin TDM is indicated, trough levels should be obtained prior to the next dialysis session. Once trough targets have been achieved, trough targets should be obtained no less than once weekly.
- If the vancomycin regimen is changed, repeat trough levels prior to the next dialysis session.

Peritoneal Dialysis (Intravenously administered Vancomycin)

	Loading Dose	Maintenance	Frequency
Peritoneal dialysis	25 – 30 mg/kg	10 – 15 mg/kg	Based on TDM
Recommended maximum loading dose o	f 3 g; recommended max	imum total daily dose of 4	l g

Trough Level Monitoring

• Given the variability of PD exchange schedules and varying degrees of residual renal output, vancomycin trough level monitoring is suggested to be carried out every 2 – 3 days.

Continuous Renal Replacement Therapy

	Loading Dose	Maintenance	Frequency
Continuous Renal	20 – 25 mg/kg	7.5 – 10 mg/kg	a12hr
Replacement Therapy (CRRT)	20 25 mg/ kg	7.5 10 mg/ kg	9±2111

Recommended maximum loading dose of 3 g; recommended maximum total daily dose of 4 g $\,$

Trough Level Monitoring

• Trough level monitoring can be carried out similar to non-dialysis patients.



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Guidance for Pharmacist-led TDM



☑ Review indication for therapy

Based on type of infection, determine if load is needed and target trough levels.

✓ Review medications

Determine if patient on any other nephrotoxic medications

☑ Monitor for nephrotoxicity: Assess for significant changes in serum creatinine

Vancomycin-induced nephrotoxicity is defined as a 50% increase serum creatinine from baseline, or an increase of 40 micromol/L. Less than 72 hours of vancomycin exposure is unlikely to cause nephrotoxicity. Patients who have significant changes in renal function in a short period of time should have increased monitoring of SCr and urine output. Additional caution should be used when dosing vancomycin in these patients.

Assessing Vancomycin TDM Level

- Determine if the trough was obtained at a pharmacokinetically appropriate time See "Trough Monitoring" section.
- ✓ Confirm trough taken at an appropriate time relative to previous dose and sample taken correctly

 Trough levels should be taken at steady state, 15 30 min prior to the dose of vancomycin. Lines should be flushed prior to drawing trough samples to prevent falsely elevated trough results.
- ✓ Verify that the patient has not missed any doses

Missed, delayed or held doses can lead to misinterpretation of trough levels.

Always maintain a Choosing Wisely Approach with respect to trough level monitoring

Frequent vancomycin dosing adjustments and over-sampling of trough levels in a short period of time can lead to subsequent inappropriate dose adjustments, and may increase the risk of patient harm.

Vancomycin TDM in Dialysis

Review dialysis schedule

When scheduling levels, consider the timing of the next dialysis session. The frequency and/or timing of monitoring may also need to be changed in the setting of shortened dialysis sessions or additional dialysis sessions.

☑ Consider the impact of residual renal output

When determining a TDM plan, take into account residual renal output as it can be a significant source of vancomycin clearance.

