Canterbury District Health Board
Te Poari Hauora o Waitaha

Antimicrobial Stewardship Bulletin

CDHB Antimicrobial Stewardship Committee
Contact: ext. 80084 or sharon.gardiner@cdhb.health.nz

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New Vancomycin dosing and monitoring Pink Book guidelines (adults)

CDHB has new **Pink Book vancomycin dosing guidelines (adults)**. Key changes include:

- **Loading dose** is now based on actual body weight (not ideal body weight).
- **Initial maintenance dose** remains guided by renal function.
- **Subsequent maintenance dosing advice** is provided by the ward pharmacist but is now based on evaluation of the vancomycin area under the concentration-time curve from 0 – 24 h (usual target AUC_{24} 400 – 600 mg/L.h).
- **Two blood samples for vancomycin concentrations are taken after the first (loading) dose** – a peak (1 – 2 hours after the end of the infusion) and a trough (within 30 minutes of the next dose). Subsequent AUC_{24} predictions will usually be done with troughs only.
- **Maximum infusion rate is now 1000 mg per hour** (not 500 mg per hour).

VANCOMYCIN

- Vancomycin IV is usually reserved for infections involving an organism (e.g. methicillin resistant *Staphylococcus aureus*) or patient (e.g. β-lactam allergy) that is not suitable for treatment with other antimicrobial agents.
- Vancomycin concentration monitoring helps optimise outcomes with this agent, which has a narrow therapeutic index and wide interindividual variation in pharmacokinetics.
- CDHB is now using an AUC_{24}-based approach to support vancomycin dosing in line with current recommendations.[1,2] Pharmacists will use computer (Bayesian) software to estimate AUC_{24} from vancomycin concentrations (similar to what is already done for aminoglycosides).

Target vancomycin AUC_{24} is 400 – 600 mg/L.h:

AUC_{24}	Potential outcome
< 400*	Emergence of MRSA resistance (vancomycin-intermediate *S. aureus*)
≥ 400*	Efficacy target
> 600	Increased risk of nephrotoxicity

**Assumes a minimum inhibitory concentration (MIC) by broth microdilution ≤1 mg/L*

- The usual target AUC_{24} range of 400 – 600 mg/L.h aims to optimise efficacy while minimising the risk of nephrotoxicity.
- An AUC_{24} ≥ 400 mg/L.h for efficacy is largely derived from retrospective observational studies of invasive infections due to MRSA with a minimum inhibitory concentration (MIC) ≤ 1 mg/L. It is not clear how it translates to other organisms or infections, but it is the best option we have currently to guide the likely effectiveness of treatment.
- An AUC_{24} > 600 mg/L.h increases the risk of nephrotoxicity but is usually well-tolerated in the short term.
- Dose adjustments based on AUC_{24} should consider the patient's clinical picture including infection (site, severity, improving/deteriorating) and assessment of renal function. Consult Infectious Diseases/Microbiology for severe infections (e.g. endocarditis, meningitis) or when the pathogen has an MIC ≥ 2 mg/L as a higher vancomycin AUC_{24} (above 600 mg/L.h) or alternative agent may be needed.
- Vancomycin dose adjustment to achieve a trough of 15 – 20 mg/L is no longer recommended at CDHB as it less reliably predicts efficacy and nephrotoxicity than AUC_{24}.

PINK BOOK ANTIMICROBIAL GUIDELINE CHANGES (ADULTS)

Vancomycin dosing guidelines

CDHB Pink Book vancomycin dosing guidelines (adults) are here, with key changes highlighted below.

Loading dose

- All adults starting vancomycin should have a loading dose to help achieve therapeutic concentrations rapidly. The loading dose is now based on actual body weight, with separate guidance offered for obese and non-obese patients.
- In severe infections dose at the upper end of the range provided – the risks of under treating during the first 24 – 48 hours of treatment outweigh the risks of overtreating.
- Vancomycin has a long infusion time – other IV antimicrobial agents with shorter infusion times should be administered first if unable to give them both concurrently.
- The prescriber should request two concentrations (peak and trough) after the first dose (see below), and advise the nurse and pharmacist that the patient is to start vancomycin.

Initial maintenance dose

- Initial maintenance dose, administered 12-hourly, remains guided by renal function. This is continued until the ward pharmacist (during regular working hours) makes further dose recommendations based on assessment of AUC_{24}.

Concentration monitoring

- Two vancomycin concentrations – a peak (1 – 2 h after the end of the infusion) and a trough (within 30 minutes of the next dose) are taken after the first (loading) dose. The computer (Bayesian) software used to estimate AUC_{24} can accommodate vancomycin concentration taken before steady-state is reached.
- Sampling after the first (rather than the third) dose will facilitate earlier dose adjustment to achieve effective vancomycin exposure. Taking an initial peak and trough enables better AUC_{24} estimates in obese or acutely unwell patients who are complex pharmacokinetically. After the loading dose, usually only trough concentrations are needed.

Infusion rate

- The maximum infusion rate for vancomycin is now 1000 mg per hour (not 500 mg per hour). Slow the infusion if signs of "red man's syndrome" occur, e.g. flushing, hypotension.

References:
1. Rybak MJ et al., Am J Health-Syst Pharm. 2020;77:835-64.
2. Drennan PG et al., Int J Antimicrob Agents 2019;53:401-7.