

## Vancomycin Intravenous Dosing and Monitoring – Adults

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|----------------------------|------------------------------------------------------------------------|
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## 1. Purpose of guideline

The purpose of this guideline is to ensure appropriate use of intravenous vancomycin and best outcomes for adult patients at Health NZ | Te Toka Tumai Auckland.

## 2. Guideline management principles and goals

All dosing of vancomycin is intravenous, as there is effectively no absorption/excretion of vancomycin across the gut wall. The only oral use for vancomycin is for treating *Clostridium difficile* disease, where serum concentration monitoring is not required.

Optimised dosing of vancomycin is based on achievement of an AUC<sub>24</sub>/MIC ratio of 400-600. A trough or pre-dose concentration of 15-20 mg/L has been used as an approximate marker of this ratio when the MIC of the organism is ≤1 mg/L, however, this is not accurate for many populations and is associated with increased adverse effects compared to AUC<sub>24</sub>-based dosing.

There is no difference in efficacy between intermittent or continuous dosing of vancomycin. The use of either approach is acceptable and should be chosen based on what is most convenient for the clinical situation.

Where dosing by weight is required, the **actual** body weight should be used.

Serum vancomycin concentrations should preferentially be obtained from a peripheral blood sample rather than a central line to reduce contamination from residual vancomycin adhering to the line.

## 3. Definitions

The following terms are used within this document.

| Term              | Definition                               |
|-------------------|------------------------------------------|
| AUC <sub>24</sub> | Area under the curve over 24 hours       |
| MIC               | Minimum inhibitory concentration         |
| IV STAT           | Single intravenous dose                  |
| ID                | Infectious Disease                       |
| SLEDD             | Slow, low-efficiency daily diafiltration |
| CVVH              | Continuous veno-venous haemofiltration   |

## 4. Intermittent dosing

### 4.1 Initial dosing

All initial intermittent doses should be determined using the vancomycin dosing calculator (Vanculator) available in Concerto tools.

The calculator will determine the patients estimated clearance and recommend an appropriate loading and maintenance dose to achieve an AUC<sub>24</sub> ≥400 from the following table:

| Loading dose       |               |
|--------------------|---------------|
| Actual body weight | Dose          |
| >100 kg            | 2.5 g IV STAT |

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| Loading dose       |               |
|--------------------|---------------|
| Actual body weight | Dose          |
| 60-100 kg          | 2 g IV STAT   |
| <60 kg             | 1.5 g IV STAT |

| Maintenance dose              |                                                        |
|-------------------------------|--------------------------------------------------------|
| Creatinine clearance (mL/min) | Dose                                                   |
| ≥150                          | 1 g IV q6h, starting six hours after loading dose      |
| 130-149                       | 1.25 g IV q8h, starting eight hours after loading dose |
| 110-129                       | 1 g IV q8h, starting eight hours after loading dose    |
| 100-109                       | 1.5 g IV q12h, starting 12 hours after loading dose    |
| 80-99                         | 1.25 g IV q12h, starting 12 hours after loading dose   |
| 70-79                         | 1 g IV q12h, starting 12 hours after loading dose      |
| 50-69                         | 750 mg IV q12h, starting 12 hours after loading dose   |
| 40-49                         | 1.25 g IV q24h, starting 24 hours after loading dose   |
| 30-39                         | 1 g IV q24h, starting 24 hours after loading dose      |
| <30                           | Discuss with ID                                        |

## 4.2 Monitoring and dose optimisation

There are two methodologies that can be used to optimise the dose of vancomycin. The preferred methodology is using Bayesian forecasting via NextDose®, whilst the alternative methodology is the traditional approach of trough/pre-dose concentration measurement. Clinical pharmacists will make dose adjustment recommendations based on the measured concentrations using NextDose®.

Serum vancomycin concentrations should be measured:

- Within 24 hours of starting therapy or any change in dosing
- At least weekly for patients with stable renal function and stable vancomycin dosing
- More frequently for unstable patients (consult ID if needed).

Documentation of the time taken and target approach (i.e., Bayesian or trough/pre-dose) when collecting the sample is mandatory.

Full blood counts, electrolytes, creatinine, and liver enzymes should be measured at least weekly for all patients on vancomycin.

| Preferred: Bayesian AUC <sub>24</sub> target |                                                                                                                                                                                                                                      |
|----------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Recommended range                            | First concentration due                                                                                                                                                                                                              |
| AUC <sub>24</sub> (target <b>400-600</b> )   | <b>Within 24 hours after loading dose</b><br>Serum concentration can be measured at any time, preferably mid-dose (Four hours post-dose) and pre-dose/trough. Doses should not be withheld while awaiting the concentration results. |

### Interpretation of result and dose adjustment

Once results are back please contact the clinical pharmacist (or on-call pharmacist after business hours) to perform AUC calculations and advise on on-going doses.

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### 4.3 NextDose©

On the NextDose© website (links are accessible through the Antimicrobial Stewardship page on HIPPO), when selecting the target, either the AUC<sub>ssDI</sub> (Area Under the steady state Concentration curve for the Dosing Interval) or C<sub>ss</sub> avg (average steady-state concentration) can be used. **Note:** the AUC<sub>24</sub> target is for a 24-hour period, so the NextDose© target should be divided across the dosing intervals, e.g., with vancomycin given 6-hourly, each AUC<sub>6</sub> target would be 100. The C<sub>ss</sub> avg target does not change with the dosing interval.

NextDose© will recommend a dose to the nearest mg to achieve the target, therefore for practicality the optimised dose should be rounded up to the nearest 250 mg using an AUC<sub>24</sub> target of 400 or rounded down if using an AUC<sub>24</sub> target of 600.

If clinical pharmacy is unavailable to assist with dose optimisation using the Bayesian method and NextDose© then a trough or pre-dose concentration can be measured and interpreted using this nomogram:

| Alternative: trough/pre-dose target        |                                                                                                                                                              |
|--------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Recommended range                          | First concentration due                                                                                                                                      |
| Pre-dose concentration (target 15-20 mg/L) | 0-2 hours before the 4th dose<br>Doses should not normally be withheld while awaiting the concentration results, subsequent doses can be modified if needed. |

| Interpretation of results and dose adjustment                                                             |                                                                                              |                                                                              |
|-----------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|
| Returned result                                                                                           | Action                                                                                       | Future monitoring                                                            |
| <b>Low concentrations (&lt;15 mg/L) – Check to see if all doses have been administered</b>                |                                                                                              |                                                                              |
| <10 mg/L                                                                                                  | <b>INCREASE dose by 50-100%</b><br>• e.g., 1 g q24h to 1 g q12h                              | Take a concentration before the 4th dose following the change.               |
| 10-15 mg/L                                                                                                | <b>INCREASE dose by 25-50%</b><br>• e.g., 1 g q12h to 1.25 g q12h<br>750 mg q24h to 1 g q24h | Take a concentration before the 4th dose following the change.               |
| 15-20 mg/L                                                                                                | Continue on current dosing regimen.                                                          | Twice weekly pre-dose concentration advised (more frequent if unstable GFR). |
| <b>High concentrations (&gt;20 mg/L) - Check to see if taken at appropriate time (0-2 hours pre-dose)</b> |                                                                                              |                                                                              |
| 20-25 mg/L                                                                                                | <b>DECREASE dose by 25-50%</b><br>• e.g., 2 g q12h to 1.5 g q12h                             | Take a concentration before the 4th dose following the change.               |
| >25 mg/L                                                                                                  | Discuss result with antimicrobial pharmacist or ID registrar.                                | Take a concentration before the 4th dose following a suggested change.       |

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## 5. Continuous dosing

### 5.1 Initial dosing

Patients should be loaded with vancomycin prior to initiation of continuous infusion. If a patient is already on intermittent dosing with therapeutic concentrations, then loading is not necessary. Patients with vancomycin concentrations <10 mg/L should be loaded as normal; 10-15 mg/L should receive 500 mg loading.

Initiate the maintenance continuous infusion as soon as the loading dose is complete.

Critically ill patients exhibit altered clearance and kinetics hence the requirement for a combined weight- and clearance-based dosing.

| Loading dose                   |                  |
|--------------------------------|------------------|
| Actual body weight             | Dose             |
| Critically unwell (any weight) | 35 mg/kg IV STAT |
| >65 kg                         | 1.5 g IV STAT    |
| <65 kg                         | 1 g IV STAT      |

| Maintenance dose              |           |              |
|-------------------------------|-----------|--------------|
| Creatinine clearance (mL/min) |           | Dose         |
| ≥150                          |           | 45 mg/kg/day |
| 120-149                       |           | 40 mg/kg/day |
| 80-119                        |           | 30 mg/kg/day |
| 50-79                         |           | 25 mg/kg/day |
| 25-49                         |           | 14 mg/kg/day |
| <25                           |           | 7 mg/kg/day  |
| SLEDD                         |           | 25mg/kg/day  |
| CVVH                          | (mL/kg/h) |              |
|                               | 10-15     | 1000 mg/day  |
|                               | 15.1-20   | 1250 mg/day  |
|                               | 20.1-25   | 1500 mg/day  |
|                               | 25.1-30   | 1750 mg/day  |
|                               | >30       | 2000 mg/day  |

### 5.2 Monitoring and dose optimisation

When continuous dosing is used the AUC<sub>24</sub> approach is utilised as a single steady-state concentration taken at any time can be multiplied by 24 to estimate AUC<sub>24</sub>.

| AUC <sub>24</sub> (CSS) target                                                                   |                                |
|--------------------------------------------------------------------------------------------------|--------------------------------|
| Recommended range                                                                                | First concentration due        |
| AUC <sub>24</sub> (target <b>400-600</b> )<br>= serum concentration (target <b>16.7-25</b> mg/L) | 24-48 hours after loading dose |

### Interpretation of results and dose adjustment

Thereafter, the daily dose can be altered proportionally to achieve the desired target concentration e.g., a concentration of 12 mg/L represents an AUC<sub>24</sub> of 288 (24 x 12), so the dose could be increased (400/288 or 1.4 fold) to achieve an AUC<sub>24</sub> of 400.

## 6. Dosing with haemodialysis

### 6.1 Initial dosing

Load patients with vancomycin as the initial dose. Subsequent dosing should be given during each dialysis session, preferably towards the last part of the treatment (e.g., Monday, Wednesday, and Friday), depending on the result of their pre-dialysis concentration.

Vancomycin is best given after dialysis but for convenience, can be given during dialysis (last part of a dialysis session). If the patient is on haemodiafiltration (HDF) treatment, then the machine mode must be switched from HDF to haemodialysis (HD) to minimise drug removal. The vancomycin infusion can be started during the remaining hours of dialysis such that the end of infusion coincides with the end of the dialysis session.

| Loading dose       |               |
|--------------------|---------------|
| Actual body weight | Dose          |
| >100 kg            | 2.5 g IV STAT |
| 60-100 kg          | 2 g IV STAT   |
| <60 kg             | 1.5 g IV STAT |

### 6.2 Monitoring

Measure serum vancomycin concentrations before the start of each dialysis session.

Blood samples should be drawn from the dialysis extracorporeal sampling port (red port, not directly from the catheter lumen) immediately after the commencement of dialysis.

Results should be available before the end of the session to inform dosing using the nomogram. If patients are consistently achieving sub-therapeutic concentrations (<15 mg/L), then interval doses should be individualised in discussion with the pharmacist.

| Interpretation of results and dose adjustment |                                      |                      |
|-----------------------------------------------|--------------------------------------|----------------------|
| Returned result                               | Next dose                            | Future monitoring    |
| <5 mg/L                                       | 2 g IV STAT at end of HD             | Before next dialysis |
| 5-15 mg/L                                     | 1.5 g IV STAT at end of HD           | Before next dialysis |
| 15-20 mg/L                                    | 1 g IV STAT at end of HD             | Before next dialysis |
| 20-25 mg/L                                    | 500 mg IV STAT after HD              | Before next dialysis |
| >25 mg/L                                      | No dose required until next dialysis | Before next dialysis |

## 7. Supporting evidence

- Baptista, J. P., Roberts, J. A., Sousa, E., Freitas, R., Deveza, N., & Pimentel, J. (2014). Decreasing the time to achieve therapeutic vancomycin concentrations in critically ill patients: developing and testing of a dosing nomogram. *Critical Care*, 18(6), 654.
- Colin, P. J., Allegaert, K., Thomson, A. H., Touw, D. J., Dolton, M., de Hoog, M., ... & Martín-Suarez, A. (2019). Vancomycin pharmacokinetics throughout life: results from a pooled

population analysis and evaluation of current dosing recommendations. *Clinical pharmacokinetics*, 58(6), 767-780.

- Drennan, P. G., Begg, E. J., Gardiner, S. J., Kirkpatrick, C. M., & Chambers, S. T. (2019). The dosing and monitoring of vancomycin: what is the best way forward?. *International journal of antimicrobial agents*, 53(4), 401-407.
- Golestaneh, L., Gofran, A., Mokrzycki, M. H., & Chen, J. L. (2009). Removal of vancomycin in sustained low-efficiency dialysis (SLED): a need for better surveillance and dosing. *Clinical nephrology*, 72(4), 286-291.
- Janssen, E. J., Väitalo, P. A., Allegaert, K., de Cock, R. F., Simons, S. H., Sherwin, C. M., ... & Knibbe, C. A. (2016). Towards rational dosing algorithms for vancomycin in neonates and infants based on population pharmacokinetic modeling. *Antimicrobial agents and chemotherapy*, 60(2), 1013-1021.
- Jeremiah, C. J., Wills, C., Bayly, A., Perry, G. J., Davis, J. S., Tong, S. Y., & Currie, B. J. (2014). Vancomycin dosing nomogram for haemodialysis patients. *Nephrology*, 19(8), 513-514.
- Reardon, N., Olsen, K., Bogard, K., Plumb, T., Yin, L., Nissen, S., ... & Peitz, G. (2012). 51: PHARMACOKINETICS OF VANCOMYCIN DURING SUSTAINED LOW-EFFICIENCY DIALYSIS. *Critical Care Medicine*, 40(12), 1-328.
- Sin, J. H., Newman, K., Elshaboury, R. H., Yeh, D. D., de Moya, M. A., & Lin, H. (2018). Prospective evaluation of a continuous infusion vancomycin dosing nomogram in critically ill patients undergoing continuous venovenous haemofiltration. *Journal of Antimicrobial Chemotherapy*, 73(1), 199-203.
- Waioneo, M. F., Kuhn, T. C., & Brown, D. L. (2015). The pharmacokinetic/pharmacodynamic rationale for administering vancomycin via continuous infusion. *Journal of clinical pharmacy and therapeutics*, 40(3), 259-265.

## 8. Associated documents

- Starship Clinical Guidelines – Vancomycin
- Medications – Prescribing
- Medications – Restricted Antimicrobials
- Medication Administration Guidelines – Vancomycin

## 9. Disclaimer

No guideline can cover all variations required for specific circumstances. It is the responsibility of the health care practitioners using this Te Toka Tumai Auckland guideline to adapt it for safe use within their own institution, recognise the need for specialist help, and call for it without delay, when an individual patient falls outside of the boundaries of this guideline.

## 10. Corrections and amendments

The next scheduled review of this document is as per the document classification table (page 1). However, if the reader notices any errors or believes that the document should be reviewed **before** the scheduled date, they should contact the owner or [Document Control](#) without delay.