**Adult Vancomycin Dosing and Monitoring Guide**

<table>
<thead>
<tr>
<th>Full Title of Guideline:</th>
<th>INTRAVENOUS VANCOMYCIN PRESCRIBING AND MONITORING GUIDELINE FOR ADULT PATIENTS</th>
</tr>
</thead>
<tbody>
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</tr>
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<td>Adult patients where Vancomycin is indicated</td>
</tr>
<tr>
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<td>Addition of a caution to review concomitant nephrotoxic drugs when starting Vancomycin</td>
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</table>

**Summary of evidence base this guideline has been created from:**

3. Vancomycin

*This guideline has been registered with the trust. However, clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt contact a senior colleague or expert. Caution is advised when using guidelines after the review date or outside of the Trust.*
INTRAVENOUS VANCOMYCIN PRESCRIBING AND MONITORING
GUIDELINE FOR ADULT PATIENTS

IMPORTANT

The Vancomycin Dosing Calculator, available on the Intranet Antibiotics Website, is recommended as the primary resource for determining the loading and starting maintenance dose for vancomycin.

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1. Introduction

Vancomycin is a glycopeptide antibiotic that is used intravenously to treat serious gram-positive infections including those caused by meticillin-resistant *Staphylococcus aureus* (MRSA). It is not systemically absorbed when taken orally. Therefore the oral route is only suitable for the treatment of *C. difficile* infection (CDI) where it exhibits a local action in the gastrointestinal tract.

Therapeutic drug monitoring of vancomycin is necessary to ensure efficacy, reduce resistance and to prevent toxicity: nephrotoxicity and ototoxicity. Over the past decade target levels have been increased in response to evidence suggesting that higher levels are required to prevent resistance and improve efficacy. Caution should be exercised in patients prescribed other nephrotoxic or ototoxic drugs. Review and consider withholding/substitution where possible. Currently, the recommended target at NUH pre-dose (‘trough’) concentration should be:

- 10–15 mg/L for standard infection
- 15–20 mg/L for deep-seated infections (e.g. osteomyelitis, endocarditis and pneumonia due to *Staphylococcus aureus*) and infections caused by less sensitive strains of MRSA (MIC ≥ 1mg/L) as advised by microbiology.

2. Vancomycin dosing regimen

The vancomycin dosing calculator available on the Antibiotics website (http://nuhnet/diagnostics_clinical_support/antibiotics/Pages/Calculators/VancomycinCalc.aspx) is recommended as the primary method for calculating the loading and starting maintenance doses. The calculator follows the below dosing regimen which is designed to achieve serum levels within the target range.

2.1. Loading dose

The single loading dose is based on actual body weight (independent of renal function/age/obesity):

Table 1 Loading-doses for vancomycin

<table>
<thead>
<tr>
<th>Patient’s Actual Body Weight</th>
<th>&lt;60kg</th>
<th>60-90kg</th>
<th>&gt;90kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single Loading dose</td>
<td>1g single dose diluted to at least 250ml, Infuse at a rate not exceeding 10mg/min* or over suggested duration of 120 minutes</td>
<td>1.5g single dose diluted to at least 500ml, Infuse at a rate not exceeding 10mg/min* or over suggested duration of 180 minutes</td>
<td>2g single dose diluted to at least 500ml, Infuse at a rate not exceeding 10mg/min* or over suggested duration of 240 minutes</td>
</tr>
</tbody>
</table>

* If using DERS (drug error reduction software programme) on the carefusion pump vancomycin can be infused at a maximum rate of 10mg/min

2.2. Maintenance dose (This should start 12-48 hours post the single loading dose- see table 2)

Estimate creatinine clearance using the Cockcroft-Gault equation or using the creatinine clearance calculator on the antibiotic website (accessed at: http://nuhnet/diagnostics_clinical_support/antibiotics/Pages/Calculators/Calc.aspx) and dose according to table 2. Do not use eGFR direct from NOTIS.
The Cockcroft-Gault equation is used to calculate creatinine clearance as an estimate of glomerular filtration rate (GFR) for the purpose of drug dosing in renal impairment:

\[
CrCl \text{ (ml/min)} = \frac{F \times (140-\text{age}) \times \text{weight (kg)}}{\text{Serum creatinine (micromol/L)}}
\]

where: 
- \( F = 1.23 \) for \( \text{♂} \)
- \( F = 1.04 \) for \( \text{♀} \)

**NOTE:**
- In patients with low serum creatinine (< 60 micromol/L), use 60 micromol/L.
- If patient is anuric, morbidly obese or in acute renal failure this equation will not give a true reflection of CrCl (for patients in acute renal failure where serum creatinine is increasing rapidly, the Cockcroft-Gault equation will overestimate their renal function, clinical judgement is required).
- For obese patients, i.e. if total body weight is more than 120% of Ideal Body Weight (IBW), “Maximum body weight” (MBW) should be used to calculate CrCl.
  - MBW = IBW x 1.2
    - IBW for males = 50 + (2.3 x (height in inches - 60))
    - IBW for female = 45 + (2.3 x (height in inches - 60))

For patients receiving CVVH discuss with critical care pharmacist / see critical care guide as additional monitoring will be required.

**Table 2 Maintenance Doses for Vancomycin**

<table>
<thead>
<tr>
<th>Calculated creatinine clearance</th>
<th>Maintenance dose</th>
<th>Time after loading to start maintenance dose (hours)</th>
<th>Recommended infusion fluid volume for each dose (either Sodium chloride 0.9% or Glucose 5%)</th>
<th>Advised duration of infusion for each dose †</th>
<th>Time of 1st vancomycin pre dose level</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;110ml/min</td>
<td>1.5g BD*</td>
<td>12</td>
<td>500ml</td>
<td>150min</td>
<td>Before 4th dose</td>
</tr>
<tr>
<td>90-110ml/min</td>
<td>1.25g BD</td>
<td>12</td>
<td>250ml</td>
<td>150min</td>
<td>Before 4th dose</td>
</tr>
<tr>
<td>75-89ml/min</td>
<td>1g BD</td>
<td>12</td>
<td>250ml</td>
<td>120min</td>
<td>Before 4th dose</td>
</tr>
<tr>
<td>55-74ml/min</td>
<td>750mg BD</td>
<td>12</td>
<td>250ml</td>
<td>90min</td>
<td>Before 4th dose</td>
</tr>
<tr>
<td>40-54ml/min</td>
<td>500mg BD</td>
<td>12</td>
<td>100ml</td>
<td>60min</td>
<td>Before 4th dose</td>
</tr>
<tr>
<td>30-39ml/min</td>
<td>750mg OD</td>
<td>24</td>
<td>250ml</td>
<td>90min</td>
<td>Before 4th dose</td>
</tr>
<tr>
<td>20-29ml/min</td>
<td>500mg OD</td>
<td>24</td>
<td>100ml</td>
<td>60min</td>
<td>Before 4th dose</td>
</tr>
<tr>
<td>10-19ml/min</td>
<td>500mg every 48 hours</td>
<td>48</td>
<td>100ml</td>
<td>60min</td>
<td>Before 2nd dose</td>
</tr>
<tr>
<td>Oliguric, anuric or &lt;10ml/min</td>
<td>Check levels 48 hours after loading dose. Re-dose with 1g once level &lt;15mg/L.</td>
<td>Only redose once levels &lt;15mg/L</td>
<td>250ml</td>
<td>120min</td>
<td>48hrs after dose</td>
</tr>
</tbody>
</table>

* Patients <45kg should be given a maximum starting dose of 1.25g BD
† If using DERS (drug error reduction software programme) on the carefusion pump vancomycin can be infused at a maximum rate of 10mg/min

**2.3 Administration**
Vancomycin MUST be administered slowly (no faster than 10mg/min) to prevent infusion-related toxicities e.g. Red man syndrome (caused by the degranulation of mast cells and basophils, resulting in the release of histamine). This typically presents as pruritus and an erythematous rash. Less frequently, hypotension, angioedema, chest pain and dyspnoea can occur. The extent of histamine release is related partly to the amount and rate of the vancomycin administration.

3. Monitoring
- Pre dose (trough) serum vancomycin concentrations are the most accurate and practical method for monitoring efficacy. Obtaining peak serum vancomycin concentrations is not necessary.
- Renal function (urine output via a fluid balance chart and at least twice weekly U+Es) should also be monitored for patients receiving more than a single dose of vancomycin.
  o Any significant reduction in renal function should lead to repeat U+Es and a pre dose vancomycin level just before the next dose is due. This result should be reviewed before any further dosing occurs (i.e. the chart endorsed level and AWAIT result).

3.1 How to take vancomycin levels
The time and date when levels are to be taken must be clearly annotated on the administration section of the vancomycin prescription and on the level request card (for more information, refer to the prescribing chapter of the NUH medicines code of practice).

If patient is oliguric/anuric/has creatinine clearance <10ml/min:
Check levels 48 hours after the initial loading dose. Do not re-dose until the level is <15mg/L.

Creatinine clearance 10-20ml/min and urine output >0.5ml/kg/hour:
- Take a pre-second dose sample.
- On the request card state the time of last dose and the time the pre dose sample was taken, details of dose and latest creatinine (without which the result cannot be interpreted).
- The dose should be given after the pre-dose level is taken if the serum creatinine is stable with good urine output. Further dosing must not continue until the result of this level is checked and documented. Results of levels are usually available within 2 hours of clinical chemistry receiving the sample 24 hours a day, 7 days per week.

Creatinine clearance >20ml/min and urine output >0.5ml/kg/hour:
- Take a pre-fourth dose sample (see table 2).
- On the request card state the time of last dose and the time the pre dose sample was taken, details of dose and latest creatinine (without which the result cannot be interpreted).
- The dose should be given after the pre-dose level is taken if the serum creatinine is stable with good urine output. Further dosing must not continue until the result of this level is checked and documented. Results of levels are usually available within 2 hours of clinical chemistry receiving the sample 24 hours a day, 7 days per week.

3.2 Target Ranges
- Minimum serum vancomycin trough concentrations should always be maintained above 10mg/L to avoid development of resistance.
- The standard target range for steady state levels is 10-15mg/L
- For deep-seated infections (endocarditis, osteomyelitis, meningitis and hospital-acquired pneumonia caused by S. aureus) and less sensitive MRSA, vancomycin serum trough concentrations of 15-20mg/L are recommended to improve penetration, increase the
probability of obtaining optimal target serum concentrations and improving clinical outcomes.

3.3. Interpretation of levels and dose adjustments

It is worth considering that steady state levels may take up to 5 dosing intervals to be achieved. Therefore, ensure that the first pre-dose level has not been taken too early; refer to table 2 for advice on when to take the first pre dose level. Ensure that the level you are interpreting is a true pre dose level and that it was taken at the correct time and that the previous dose has not been significantly delayed/omitted and that renal function has been monitored as per section 3 and Table 2.

Table 3 Maintenance dose adjustment using Pre-dose steady state vancomycin levels - excluding patients with CrCl <10ml/min, anuria or oligouria (for these patients see table 2 for advice on re-dosing).

<table>
<thead>
<tr>
<th>Pre-dose (trough) level</th>
<th>Guidance on how to adjust the maintenance dose given in Table 2</th>
<th>When to take subsequent level (if renal function stable)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 5mg/L</td>
<td>Increase the dose by two dosing levels from current dosing schedule (e.g. if current dose is 500mg BD move <strong>UP</strong> Table 2 by two rows to increase dose to 1g BD)#</td>
<td>Pre-4&lt;sup&gt;th&lt;/sup&gt; dose</td>
</tr>
<tr>
<td>5-10 mg/L</td>
<td>Increase dose by one dosing level#</td>
<td>Pre-4&lt;sup&gt;th&lt;/sup&gt; dose</td>
</tr>
<tr>
<td>10-15 mg/L</td>
<td>Aiming for 10-15mg/L - Continue at current dose.</td>
<td>After 3-4 days</td>
</tr>
<tr>
<td></td>
<td>Aiming for 15-20mg/L - Increase by one dosing level#</td>
<td>Pre-4&lt;sup&gt;th&lt;/sup&gt; dose</td>
</tr>
<tr>
<td>15-20mg/L</td>
<td>Aiming for 10-15mg/L - Decrease by one dosing level without omitting any doses (i.e. move <strong>DOWN</strong> Table 2 by one row).*</td>
<td>Pre-4&lt;sup&gt;th&lt;/sup&gt; dose</td>
</tr>
<tr>
<td></td>
<td>Aiming for 15-20mg/L - Continue at this dose.</td>
<td>After 3-4 days</td>
</tr>
<tr>
<td>20-25mg/L</td>
<td>Decrease by one dosing level without omitting any doses*</td>
<td>Pre-4&lt;sup&gt;th&lt;/sup&gt; dose</td>
</tr>
<tr>
<td>25-30 mg/L</td>
<td>Omit next dose. Decrease by two dosing levels. Repeat U+Es *</td>
<td>Pre-4&lt;sup&gt;th&lt;/sup&gt; dose. If renal function unstable check level the next day before further dosing.</td>
</tr>
<tr>
<td>More than 30mg/L</td>
<td><strong>Omit any further doses.</strong> Re-check renal function (i.e. U+Es) and urine output and review the need for vancomycin treatment. Check levels daily until they are back within the target range and decrease by at least two dosing levels. If further advice is required, contact microbiology / pharmacy <strong>within normal working hours only.</strong></td>
<td></td>
</tr>
</tbody>
</table>

* if current regimen is 500mg every 48 hours – seek advice from microbiology / pharmacy.
# if increasing the dose would result in a dose larger than 1.5g twice a day – seek advice from Microbiology for an alternative agent.