NHS Grampian Staff Guidance for the Administration of Intravenous Vancomycin in Adults via Intermittent (pulsed) Infusion

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Acute Sector

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Operational Management Unit: Unit Operational Managers

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<td>Major changes to dosing protocol following new recommendations on target trough levels.</td>
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</tr>
</tbody>
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**NHS Grampian Staff Guidance for the Administration of Intravenous Vancomycin in Adults via Intermittent (pulsed) Infusion**

**Contents**

- Introduction and Rationale ................................................................................................... 2
- Exclusions: ........................................................................................................................... 2
- Cautions: .............................................................................................................................. 3
- Vancomycin Administration .................................................................................................. 3
- Prescribing and documentation ........................................................................................... 3
- **STEP 1: Calculate and prescribe the loading dose and maintenance dose of vancomycin.** 4
- Box 1: Estimation of creatinine clearance (CrCl) ................................................................. 4
- Loading Infusion .................................................................................................................. 4
- Table 1: Initial Vancomycin LOADING Dose ........................................................................ 4
- Maintenance Dosage Regimen ............................................................................................ 5
- Table 2: Vancomycin MAINTENANCE dosage regimen ...................................................... 5
- **STEP 2: Monitor the vancomycin concentration and reassess the dose** ............................. 5
- Target trough vancomycin concentrations ......................................................................... 6
- Adjustment of the vancomycin dosage regimen .................................................................. 6
- If the measured concentration is unexpectedly HIGH or LOW............................................. 6
- Table 3: Adjustment of Vancomycin dosage regimen .......................................................... 6
- General points ..................................................................................................................... 7
- Box 2: Toxicity ..................................................................................................................... 7
- **STEP 3: Assess daily the ongoing need for vancomycin and for signs of toxicity** ............. 7
- References .......................................................................................................................... 7
- Consultation List .................................................................................................................. 8
- Appendix 1: VANCOMYCIN intravenous infusion prescription and administration record ... 9
- Appendix 2: Maximum Body Weight table – for creatinine clearance calculations............. 11

**Glossary of abbreviations**

- ABW: Actual body weight
- CrCl: Creatinine Clearance
- eGFR: estimated Glomerular Filtration Rate
- IBW: Ideal body weight
- MBW: Maximum Body Weight
- MIC: Minimum Inhibitory Concentration
- MRSA: Meticillin-resistant *Staphylococcus aureus*
- NSAIDs: Non-steroidal anti-inflammatory drugs
Acute Sector
NHS Grampian Staff Guidance for the Administration of Intravenous Vancomycin in Adults via Intermittent (pulsed) Infusion

Introduction and Rationale

This protocol details the dosing, prescribing, monitoring and administration of intravenous vancomycin as an intermittent (pulsed) infusion.

Vancomycin is a glycopeptide antibacterial used in the treatment of serious staphylococcal or other Gram-positive infections when other drugs such as the penicillins cannot be used because of resistance or patient intolerance. It is used particularly in the treatment of meticillin-resistant staphylococcal infections (MRSA). Refer to NHSG Infection Management Guidelines: Empirical Antibiotic Therapy for indications.

Vancomycin can also be administered as a continuous infusion, when practical, for patients with severe or deep-seated infections (e.g. pneumonia, endocarditis, bone and joint infections). In NHS Grampian only Intensive care use continuous infusion.

Vancomycin works most effectively when the levels of the drug remain above the minimum inhibitory concentration (MIC) for the target organism at all times. Trough levels of vancomycin therefore require to be monitored throughout treatment and these should be 10-15mg/L in standard infections. On the basis of the potential to improve penetration, to increase the probability of optimal target serum concentrations, and to improve the clinical outcomes of complicated infections, such as bacteraemia, endocarditis, osteomyelitis, meningitis and hospital-acquired pneumonia caused by S. aureus, trough serum vancomycin concentrations of 15-20mg/L are recommended. This range is also recommended for less sensitive strains of S. aureus.

Exclusions:

This guidance is only for use in adults over 16 years of age.

Advice should be sought from Microbiology or an Infection Specialist on treatment options if the patient has any of the following exclusions:

- Patients treated in renal units or receiving haemodialysis or haemofiltration (contact the Renal unit for advice and follow the local unit protocol)
- Patients who are allergic/hypersensitive to vancomycin
- Patients with previous hearing loss
- Patients in intensive care who require a continuous vancomycin infusion
- Treatment of Clostridium difficile Infection (vancomycin should be given orally)
- Treatment of ventriculitis or ventriculoperitoneal shunt infections (contact neurology specialist for advice).
Cautions:

Use with caution in patients with teicoplanin sensitivity due to possibility of cross-
sensitivity.
Concurrent administration of neurotoxic and / or nephrotoxic agents increases the
risk of vancomycin toxicity. Review therapy and consider amending or withholding
nephrotoxic drugs during treatment with vancomycin,
Where possible, avoid co-administration with:
  o  gentamicin (aminoglycosides)
  o  NSAIDs
  o  amphotericin
  o  potent diuretics
  o  ACE inhibitors.

This list is not exhaustive – consult the Summary of Product Characteristics (SPC)
for a full list (www.medicines.org.uk).

Vancomycin Administration

Vancomycin is very irritating to tissue, and should not be given intramuscularly as
this causes injection site necrosis. It must be given by slow intravenous infusion
using a dilute solution to reduce the risk of tissue necrosis if extravasation occurs.
Vancomycin should not be given rapidly due to the risk of infusion reactions.
The intravenous use of vancomycin may be associated with the so-called 'red-neck'
or 'red-man' syndrome, characterised by erythema, flushing, or rash over the face
and upper torso, and sometimes by hypotension and shock-like symptoms. The
effect appears to be due in part to the release of histamine and is usually related to
rapid infusion 1. It may also cause pain or muscle spasm.

In order to avoid these risks:
  •  Vancomycin must ALWAYS be administered by intravenous INFUSION in
    either 0.9% Sodium Chloride or 5% Glucose
  •  Final concentration: NOT MORE THAN 5mg/mL for peripheral administration
  •  Rate of infusion: NO FASTER THAN 10mg/min 6

Prescribing and documentation

Vancomycin should be prescribed on the Adult Vancomycin Intravenous Infusion Prescription
and Administration record (Appendix 1), and reference to this should be made on the
patient’s main prescription chart as shown below and opposite:
STEP 1: Calculate and prescribe the loading dose and maintenance dose of vancomycin

- To reduce the risk of mortality, commence vancomycin administration within 1 hour of recognising sepsis

- If creatinine is known – use the online calculator (preferred method). The guidance in Table 1 (Initial LOADING dose) and Table 2 (MAINTENANCE dose) can be used if the online calculator is not available. The dose amount and dosage interval are based on estimated creatinine clearance (Box 1) and actual body weight.

- If creatinine is not known – calculate and prescribe a loading dose based on actual body weight (Table 1). Calculate the maintenance dose once the creatinine is available.

Box 1: Estimation of creatinine clearance (CrCl)

The following ‘Cockcroft Gault’ equation can be used to estimate creatinine clearance (CrCl):

\[ \text{CrCl} = \frac{[140-\text{age (years) }] \times \text{weight}^{*} \text{ (kg)}}{\text{serum creatinine}^{\dagger} \text{(micromol / L)}} \times 1.23 \text{ (male) or 1.04 (female)} \]

Cautions:
- *Use actual body weight or maximum body weight for patient’s height, whichever is lower. For maximum body weight see Appendix 2 or: http://www.scottishmedicines.org.uk/files/sapg/Maximum_body_weight_table.pdf
- ^In patients with low creatinine (<60micromol/L), use 60 micromol/L to avoid overestimating creatinine clearance due to low muscle mass.
- Note: Use of estimated glomerular filtration rate (eGFR) from labs is not recommended for calculation of vancomycin doses.

Loading Infusion

Table 1: Initial Vancomycin LOADING Dose

<table>
<thead>
<tr>
<th>Actual Body Weight (ABW)</th>
<th>Dose (0.9% Sodium Chloride)</th>
<th>Volume (0.9% Sodium Chloride)</th>
<th>Duration of infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40kg</td>
<td>750mg</td>
<td>250mL</td>
<td>1.5 hours</td>
</tr>
<tr>
<td>40-59kg</td>
<td>1000mg</td>
<td>250mL</td>
<td>2 hours</td>
</tr>
<tr>
<td>60-90kg</td>
<td>1500mg</td>
<td>500mL</td>
<td>3 hours</td>
</tr>
<tr>
<td>&gt;90kg</td>
<td>2000mg</td>
<td>500mL</td>
<td>4 hours</td>
</tr>
</tbody>
</table>

^Glucose 5% can be used in patients with sodium restriction.
Maintenance Dosage Regimen

- Give the first maintenance infusion 12, 24 or 48 hours after the loading infusion according to dose interval provided by the online calculator or Table 2 (below).

Table 2: Vancomycin MAINTENANCE dosage regimen

<table>
<thead>
<tr>
<th>CrCl (mL/min)</th>
<th>Dose</th>
<th>Dosing Interval</th>
<th>Volume of sodium chloride 0.9%‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 20</td>
<td>500mg over 1 hour</td>
<td>48 hours</td>
<td>250mL</td>
</tr>
<tr>
<td>20-29</td>
<td>500mg over 1 hour</td>
<td>24 hours</td>
<td>250mL</td>
</tr>
<tr>
<td>30-39</td>
<td>750mg over 1.5 hours</td>
<td>24 hours</td>
<td>250mL</td>
</tr>
<tr>
<td>40-54</td>
<td>500mg over 1 hour</td>
<td>12 hours</td>
<td>250mL</td>
</tr>
<tr>
<td>55-74</td>
<td>750mg over 1.5 hours</td>
<td>12 hours</td>
<td>250mL</td>
</tr>
<tr>
<td>75-89</td>
<td>1000mg over 2 hours</td>
<td>12 hours</td>
<td>250mL</td>
</tr>
<tr>
<td>90-110</td>
<td>1250mg over 2.5 hours</td>
<td>12 hours</td>
<td>250mL</td>
</tr>
<tr>
<td>&gt;110</td>
<td>1500mg over 3 hours</td>
<td>12 hours</td>
<td>500mL</td>
</tr>
</tbody>
</table>

‡ Glucose 5% may be used in patients with sodium restriction.

- Doses up to 2000mg can be diluted in 500mL fluid.
- The daily dose can be split into 3 equal doses and given 8 hourly. This approach is especially useful for patients who require high doses as it produces higher trough concentrations, and reduces the time of each individual infusion. For example, 1500mg 12 hourly (3000mg per day) could be prescribed as 1000mg 8 hourly, and 750mg 12 hourly (1500mg per day) as 500mg 8 hourly. For further advice discuss with Pharmacist or microbiology.

STEP 2: Monitor the vancomycin concentration and reassess the dose

Concentrations are meaningless unless the dose and sample times are recorded accurately.

- Due to wide variability in the handling of vancomycin, early analysis of a vancomycin concentration is required to ensure that the dosage regimen is appropriate.
- Take a trough sample (pre-dose) within 24-48 hours of starting therapy then every 2-3 days, or daily if the patient has unstable renal function.
- Monitor creatinine daily.
- Record the exact time of all vancomycin samples on the Vancomycin Intravenous Infusion Prescription and Administration record AND on the sample request form along with the last time of administration.
- If the renal function is stable, give the next dose before the trough result is available. If renal function is deteriorating, withhold until the result is available then follow the advice in Table 3.
Target trough vancomycin concentrations

- Target trough concentration range: 10 – 20mg/L
- If the patient is seriously ill (severe or deep-seated infection), the target trough concentration range is 15 - 20mg/L. If the measured concentration is <15mg/L, consider increasing the dose amount or reducing the dosage interval (see 8 hourly dosing above).
- If the patient is failing to respond, seek advice from microbiology or an infection specialist.

Adjustment of the vancomycin dosage regimen

- Always check that the dosage history and sampling time are appropriate before interpreting the result.
- Seek advice from pharmacy or microbiology if you need help to interpret the result.

If the measured concentration is unexpectedly HIGH or LOW

If the measured concentration is unexpectedly HIGH or LOW, consider the following:

- Were the dose and sample times recorded accurately?
- Was the correct dose administered?
- Was the sample taken from the line used to administer the drug?
- Was the sample taken during drug administration?
- Has renal function declined or improved?
- Does the patient have oedema or ascites?

Table 3: Adjustment of Vancomycin dosage regimen

<table>
<thead>
<tr>
<th>Vancomycin Concentration</th>
<th>Suggested Dose Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10mg/L</td>
<td>Increase dose by 50% and consider reducing the dosage interval or seek advice</td>
</tr>
<tr>
<td>10-15mg/L</td>
<td>If the patient is responding, maintain the present dosage regimen</td>
</tr>
<tr>
<td></td>
<td>If the patient is seriously ill, consider increasing the dose amount or reducing the dosage interval to achieve a trough level of 15-20mg/L</td>
</tr>
<tr>
<td>15 - 20mg/L</td>
<td>Maintain the present dosage regimen</td>
</tr>
<tr>
<td>&gt;20mg/L</td>
<td>Stop until &lt;20mg/L and seek advice</td>
</tr>
</tbody>
</table>

If in doubt, take another sample before modifying the dosage regimen and / or contact pharmacy for advice.
General points

- Record the exact times of all measured concentrations on the Vancomycin Intravenous Infusion Prescription and Administration record.
- Undertake pre-prescribing checks (Box 2) to assess the risk of toxicity.
- Reassess the dose and continue or prescribe a dosage change.
- Document the action taken in the medical notes and on the Vancomycin Intravenous Infusion Prescription and Administration record.
- Review the need for vancomycin daily.

Box 2: Toxicity

- Monitor creatinine daily. Seek advice if renal function is unstable (e.g. a change in creatinine of > 15-20%).
- Signs of renal toxicity include increase in creatinine or decrease in urine output / oliguria.
- Consider an alternative agent if creatinine is rising or the patient becomes oliguric.
- Vancomycin may increase the risk of aminoglycoside induced ototoxicity – use caution if co-prescribing.

STEP 3: Assess daily the ongoing need for vancomycin and for signs of toxicity

- Review the need for vancomycin daily.
- Consider adjusting the dose regimen or using an alternative agent if renal function changes. Signs of renal toxicity include increase in creatinine or decrease in urine output/oliguria.
- Consider changing to an oral alternative – refer to the IV to Oral switch (IVOST) policy.

For further advice contact:
Antibiotic Pharmacists Bleep 2937, Ext: 51048.
Ward Clinical Pharmacists - see ward information for contact details.
Medical Microbiology bleep 2321 or contact switchboard.

References


Consultation List
Dr V. Bateman  Specialist Registrar, Infectious Diseases
Dr C. Brunton  Renal Consultant
Dr G. Douglas  Infectious Diseases Consultant
Dr N. ElSakka  Specialist Registrar, Infectious Diseases
Dr N. Fluck    Renal Consultant
Dr I. Gould    Medical Microbiology Consultant
Ms P. Harrison Infection Control Manager
Dr A. Karcher  Infection Prevention and Control Doctor
Dr. I Khan     Renal Consultant
Dr R. Laing    Infectious Diseases Consultant
Dr A. Mackenzie Infectious Diseases Consultant
Dr C. Miller   Renal Consultant
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Dr D. O'Brien  Infection Prevention and Control Doctor
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All acute sector Pharmacists, NHS Grampian

Comments received from:
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Margaret Fernie  Senior Pharmacist, ARI
Janet Hasell    ICU Pharmacist, ARI
Jenny Mosley    Paediatric Pharmacist, RACH
Appendix 1: VANCOMYCIN intravenous infusion prescription and administration record

<table>
<thead>
<tr>
<th>VANCOMYCIN intravenous infusion prescription and administration record – see overleaf for guidance on calculations</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th><strong>Patient Name:</strong></th>
<th><strong>Gender:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>D.O.B:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>CHI:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Ward:</strong></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Vancomycin Loading Dose for ALL patients (given ONCE only)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Date</strong></td>
</tr>
<tr>
<td>-----------</td>
</tr>
<tr>
<td><strong>Note:</strong> Please refer to guidance overleaf for rate of administration and dilution of vancomycin dose.</td>
</tr>
</tbody>
</table>

**Further prescription sheet if required:**

<table>
<thead>
<tr>
<th><strong>Vancomycin Maintenance Dose</strong></th>
<th><strong>Date</strong></th>
<th><strong>Time</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medicine</strong></td>
<td><strong>08</strong></td>
<td><strong>08</strong></td>
</tr>
<tr>
<td><strong>Route</strong></td>
<td><strong>IV</strong></td>
<td><strong>IV</strong></td>
</tr>
<tr>
<td><strong>Dose</strong></td>
<td><strong>12</strong></td>
<td><strong>12</strong></td>
</tr>
<tr>
<td><strong>Signature/Print name</strong></td>
<td><strong>14</strong></td>
<td><strong>14</strong></td>
</tr>
<tr>
<td><strong>Start date</strong></td>
<td><strong>18</strong></td>
<td><strong>18</strong></td>
</tr>
<tr>
<td><strong>Pharm</strong></td>
<td><strong>20</strong></td>
<td><strong>20</strong></td>
</tr>
<tr>
<td><strong>Additional instructions</strong></td>
<td><strong>22</strong></td>
<td><strong>22</strong></td>
</tr>
</tbody>
</table>

**Is dosage change required based on trough level? If Yes, start new prescription sheet:**

<table>
<thead>
<tr>
<th><strong>Trough level (mg/L)</strong></th>
<th><strong>Y/N</strong></th>
<th><strong>Y/N</strong></th>
<th><strong>Y/N</strong></th>
<th><strong>Y/N</strong></th>
<th><strong>Y/N</strong></th>
<th><strong>Y/N</strong></th>
</tr>
</thead>
</table>

**Baseline Prescribing Information**

Must be completed before prescribing dose.

**Target Trough Concentration:**

- **Actual Body Weight:** kg
- **Height:** cm
- **Ideal Body Weight:** kg
- **Serum Creatinine:** mmol/L
- **Maximum Clearance:** ml/min
- **Loading Dose:** mg
- **Maintenance Dose:** mg
- **Dosing Interval:** hours
- **Date:** Sign:
Appendix 1: VANCOMYCIN intravenous infusion prescription and administration record (cont’d)

NHS Crampton Summary of Protocol for the Administration of Intravenous VANCOMYCIN in Adults via Intermittent Infusion

1. **Vancomycin Loading Dose** (*no adjustment for loading if obese*)

<table>
<thead>
<tr>
<th>Actual body weight (kg)</th>
<th>Dose (mg)</th>
<th>Volume of sodium chloride 0.9% or glucose 5% (ml)</th>
<th>Duration of Infusion (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 – 59 kg</td>
<td>1000 mg</td>
<td>250 ml</td>
<td>2 hours</td>
</tr>
<tr>
<td>60 – 80 kg</td>
<td>1500 mg</td>
<td>500 ml</td>
<td>3 hours</td>
</tr>
<tr>
<td>&gt; 80 kg</td>
<td>2000 mg</td>
<td>750 ml</td>
<td>4 hours</td>
</tr>
</tbody>
</table>

2. **Maintenance Vancomycin Dose**

<table>
<thead>
<tr>
<th>CRI (mL/min)</th>
<th>Dose &amp; infusion rate (mg/min)</th>
<th>Volume (ml)</th>
<th>Dosing Interval (hours)</th>
<th>Time to take first trough level</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 20</td>
<td>500 mg over 1 hr</td>
<td>250 ml</td>
<td>48 hours</td>
<td>Before 2nd dose</td>
</tr>
<tr>
<td>20 – 29</td>
<td>500 mg over 1 hr</td>
<td>250 ml</td>
<td>24 hours</td>
<td>Before 3rd dose</td>
</tr>
<tr>
<td>30 – 39</td>
<td>750 mg over 1.5 hr</td>
<td>250 ml</td>
<td>24 hours</td>
<td>Before 3rd dose</td>
</tr>
<tr>
<td>40 – 59</td>
<td>500 mg over 1 hr</td>
<td>250 ml</td>
<td>12 hours</td>
<td>Before 4th dose</td>
</tr>
<tr>
<td>50 – 74</td>
<td>750 mg over 1.5 hr</td>
<td>250 ml</td>
<td>12 hours</td>
<td>Before 4th dose</td>
</tr>
<tr>
<td>75 – 99</td>
<td>1000 mg over 2 hr</td>
<td>250 ml</td>
<td>12 hours</td>
<td>Before 4th dose</td>
</tr>
<tr>
<td>100 – 110</td>
<td>1250 mg over 2.5 hr</td>
<td>250 ml</td>
<td>12 hours</td>
<td>Before 4th dose</td>
</tr>
<tr>
<td>&gt; 110</td>
<td>1500 mg over 3 hr</td>
<td>500 ml</td>
<td>12 hours</td>
<td>Before 4th dose</td>
</tr>
</tbody>
</table>

NB. For 12 hourly regimes the daily dose can be split into 3 equal doses and given 8 hourly e.g. 1000mg 8 hourly could be given as 1000mg 8 hourly

3. **Monitoring of Vancomycin Concentrations**

- Target concentration (trough at end of dosage interval):
  - Standard: 10 – 15mg/L
  - Severe or deep-seated infections: 15 – 20mg/L
- Take a trough (pre-dose) sample before 4th dose for patients on a 12 hourly regimen, before 3rd dose for 24 hourly regimen, and before 2nd dose for 48 hourly regimen, then every 2 to 3 days. Take samples daily if the patient has unstable renal function.
- Monitor creatinine regularly, usually twice weekly, unless unstable when more frequent monitoring is indicated.

4. **Adjustment of Vancomycin Doses**

- Always check that the dosage history and sampling time are appropriate before interpreting the result.

<table>
<thead>
<tr>
<th>Vancomycin Concentration</th>
<th>Suggested Dose Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 10 mg/L</td>
<td>Increase by 50% (up to max 1.5g twice daily) or see advice</td>
</tr>
<tr>
<td>10 – 20 mg/L</td>
<td>Maintain the present dose</td>
</tr>
<tr>
<td>&gt; 20 mg/L</td>
<td>Stop until ≤20 mg/L and see advice</td>
</tr>
</tbody>
</table>

Seek advice from your clinical pharmacist, the antibiotic pharmacist, or medical microbiology if you need help to interpret the result or adjust dosing.
Appendix 2: Maximum Body Weight table – for creatinine clearance calculations

This table can be used to determine whether patients are classed as ‘obese’ (>20% over Ideal Body Weight) and to determine the Maximum Body Weight for use in the Cockcroft Gault equation (see Box 1).

<table>
<thead>
<tr>
<th>Height (ft inches)</th>
<th>Height (cm)</th>
<th>MBW (kg) MALE</th>
<th>MBW (kg) FEMALE</th>
</tr>
</thead>
<tbody>
<tr>
<td>4' 8&quot;</td>
<td>142</td>
<td>49</td>
<td>43</td>
</tr>
<tr>
<td>4' 9&quot;</td>
<td>145</td>
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