IV Vancomycin dosing and monitoring Antibiotic Guidelines

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Applies to: Salford Royal Care Organisation
Approving Committee Medicines Management Group
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1. **Overview** *(What is this guideline about?)*

This guideline gives recommendations for IV vancomycin dosing using intermittent intravenous infusions. There is a separate vancomycin continuous infusion guide for patients in intensive care. Continuous infusions should not be used outside the Critical care and Neurosurgical settings.

This guideline and the dosing calculator are a guide to initial dosing but individual patient assessment involving discussion with pharmacy +/- microbiology may be required.

2. **Scope** *(Where will this document be used?)*

This policy applies to all clinical staff involved the prescribing of antimicrobials.

**Associated Documents**

- 144TD(C)25(A5) - Issue No 3.1 - Antimicrobial Stewardship Policy  
- 163TD(C)(33) – Issue No. 14 - Medicines Policy  

3. **Background** *(Why is this document important?)*

Antimicrobial agents are among the most commonly prescribed drugs and account for 20% of the hospital pharmacy budget. Unfortunately, the benefits of antibiotics to individual patients are compromised by the development of bacterial drug resistance. Resistance is a natural and inevitable result of exposing bacteria to antimicrobials.

Good antimicrobial prescribing will help to reduce the rate at which antibiotic resistance emerges and spreads. It will also minimise the many side effects associated with antibiotic prescribing, such as Clostridium difficile infection. It should be borne in mind that antibiotics are not needed for simple coughs and colds. In some clinical situations, where infection is one of several possibilities and the patient is not showing signs of systemic sepsis, a wait and see approach to antibiotic prescribing is often justified while relevant cultures are performed.

This document provides treatment guidelines for the most common situations in which antibiotic treatment is required. The products and regimens listed here have been selected by the Trust's Medicines Management Group on the basis of published evidence. Doses assume a weight of 60-80kg with normal renal and hepatic function. Adjustments may be needed for the treatment of some patients.

This document provides treatment guidelines for the appropriate use of antibiotics. The recommendations that follow are for empirical therapy and do not cover all clinical circumstances. Alternative antimicrobial therapy may be needed in up to 20% of cases. Alternative recommendations will be made by the microbiologist in consultation with the clinical team.
This document refers to the treatment of adult patients (unless otherwise stated).

Refer to up to date BNF/SPC for information on interactions, side effects, cautions and contraindications for individual drugs.

4. What is new in this version?

- Additional guidance has been included on what to do if the levels obtained are too low or too high.
- Advice on when to take a level in renal dosing added. This information is already on the vancomycin TDM order set in EPR.

5. Guideline

Glycopeptides are used in the treatment of infections caused by Staphylococci, including MRSA, and Streptococci.

Note – there is a separate vancomycin continuous infusion guide for patients in intensive care. Continuous infusions should not be used outside the Critical care and Neurosurgical settings.

5.1 Method of administration

There are two methods of administering intravenous vancomycin, INTERMITTENT INTRAVENOUS INFUSIONS or CONTINUOUS INTRAVENOUS INFUSION.

The continuous intravenous infusion should ONLY be used in Critical Care or on the Neurosurgical wards.

5.2. Dose calculation

Vancomycin is almost completely eliminated unchanged in urine by glomerular filtration (>90%) Renal function is the most important factor in determining dose and frequency.

A dosing calculator is available for the calculation of renal function and vancomycin dose. Patients weight, height and serum creatinine (or measured creatinine clearance if available) are required to use the calculator.

VANCOMYCIN CALCULATOR

For background information on the vancomycin dosing calculator refer to Section 5.6.
5.3. Patients with Renal failure/Kidney disease (CrCl≤30ml/min or dialysis)

Vancomycin should be given at extended intervals to maintain therapeutic concentrations.

Current clinical practice is to administer vancomycin as a stat dose of 1000 milligrams and closely monitor. Vancomycin level should be obtained 24 hours after the first dose is given. The patient can be re-prescribed a stat dose when the vancomycin trough concentration is below 20mg/L.

Seek specialist advice from renal/antibiotic pharmacists for patients with end stage kidney disease and/or dialysis. Renal transplant patients should be treated according to their current renal function.

5.4 Therapeutic drug level monitoring

5.4.1. Intermittent IV infusions

Serum antibiotic levels should be measured in all patients who have treatment with intravenous vancomycin for longer than 48 hours.

The sample should be taken immediately before the fourth dose or after 48 hours of therapy.

A trough (pre-dose) sample only is required. The exact time that the sample is drawn should be recorded. The exact time that a dose of vancomycin is administered should also be recorded.

For patients with CrCl≥30mls/min the next (fourth) dose should be given and the result used to change further doses if necessary.

The target range for vancomycin pre-dose concentrations in ALL patients on intermittent vancomycin in SRCO is 15-20mg/L.

The rationale for a single target range for intermittent dosing is as follows:

- Simpler for prescribers and will reduce risk of incorrect target range being used (prior incidents in SRCO where lower range inappropriately chosen)

- Most infections being treated with IV vancomycin would be classed as severe/deep and require higher target range anyway. The only exceptions to this would be urinary tract infection (an uncommon situation), or skin and soft tissue infection in non-obese, non-swollen limb (again relatively uncommon).

- The risk of underdosing or using the incorrect target range was felt to be a bigger risk that the risk of toxicity from occasional higher dosing of vancomycin. Local experience shows several cases where underdosing of vancomycin is a more common problem than excess dosing.
If a level is outside of the normal range, please refer to table below:

<table>
<thead>
<tr>
<th>Vancomycin level too LOW</th>
<th>•Check that all doses have been given as prescribed.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>•If trough level appears genuine, use the <a href="#">vancomycin dose adjustment calculator</a> to obtain a new dosage regime.</td>
</tr>
<tr>
<td>Vancomycin level too HIGH</td>
<td>•Check that the level has been taken at the correct time. High levels may occur due to levels being taken too early.</td>
</tr>
<tr>
<td></td>
<td>•Check where the blood sample was taken from – falsely high levels can be obtained from samples taken from the same line that the drug was infused through</td>
</tr>
<tr>
<td></td>
<td>•Check the patient’s renal function. An increase in trough level may coincide with decreased creatinine clearance</td>
</tr>
<tr>
<td></td>
<td>•If the high trough level appears genuine, use the <a href="#">vancomycin dose adjustment calculator</a> to obtain a new dosage regime. Consider omitting dose based on the level:</td>
</tr>
<tr>
<td></td>
<td>- If vancomycin trough level is 20-25mg/L, give new dosage regime without omitting any doses. Take a level before the 4th new dose.</td>
</tr>
<tr>
<td></td>
<td>- If vancomycin trough level is &gt;25mg/L, the new dosage regime should be withheld until repeat vancomycin levels are back in the therapeutic range.</td>
</tr>
</tbody>
</table>

If a dose alteration occurs, trough levels should be measured again, after a further 3 doses have been given.

If no dose alteration is made, a re-assay interval of 6 days is acceptable if renal function is normal but assays will need to be done more frequently if there is renal impairment, elevated trough levels, or co-administration of potentially nephrotoxic drugs.

**Pharmacokinetics and Dosage Adjustment**

*There are a number of available nomograms for dosing of vancomycin. Due to pharmacokinetic variability, serum concentrations should be used to ensure therapeutic levels are reached and toxicity avoided.*

In most patients vancomycin exhibits linear kinetics. Linear dose, proportional pharmacokinetics can be used to alter doses based on trough levels:

\[
\text{New dose} = \frac{\text{Target level at steady state}}{\text{Current level at steady state}} \times \text{Old dose}
\]

Ie: a doubling of the dose, should double the serum level.
5.4.2. Continuous IV Infusion

The target level for continuous vancomycin infusion is 15-25mg/L. Please note that this is higher than for conventional intermittent dosing regimens.

Request a serum vancomycin level every day at 08:00 hrs with the routine bloods and send urgently to Clinical Biochemistry.

Until the patient’s vancomycin dose is stable, levels must be taken daily. Once stable, alternate days’ levels are sufficient.

Do not take levels if the vancomycin has been started within the last 6 hours, i.e. after 2:00am; instead, wait until the following morning to check levels.

Adjust the maintenance infusion dose (by altering the infusion rate) according to the serum levels, using the Continuous IV infusion dose adjustment calculator.

The new infusion rate must be prescribed on EPMAR.

5.5 Vancomycin hypersensitivity

Vancomycin may cause hypersensitivity reactions by several different mechanisms. The most common of these is the red man syndrome, which is an idiopathic infusion reaction characterised by flushing, erythema and itching, that can affect the upper body, neck and face. Chest and back pain, dyspnoea, hypotension, shock, and rarely cardiac arrest may also occur.

Red man syndrome is related to the rate of administration. It is common when vancomycin is administered at a rate of 1g in ≤ 60 minutes.

The rate of infusion must not exceed 10mg/min.

Red man syndrome may be more likely to occur when vancomycin is given in combination with opioids. Vancomycin hypersensitivity may also be due to IgE-mediated anaphylaxis and either maculo-papula or urticarial skin rashes; anaphylaxis or cutaneous forms of hypersensitivity are rare.

Infusion related events usually resolve within 20 minutes but may persist for several hours.

5.6 Vancomycin dosing calculator – Background information

Loading dose

The Initial treatment dose below is recommended to promptly achieve adequate therapeutic concentrations of vancomycin in all patients irrespective of renal function.

The Initial loading dose should be based on the patient’s actual body weight. Fluid balance (over or under hydration) is not an important factor in drug distribution.

Administration:
Doses should be given in 0.9% NaCl 250mls at a rate not exceeding 10mg/min.
It is your responsibility to check on the intranet that this printed copy is the latest version

Loading/ initial doses must be prescribed for immediate administration as a *stat* dose

<table>
<thead>
<tr>
<th>Patient’s actual Body Weight</th>
<th>Loading dose (milligrams)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 60 kg</td>
<td>1000</td>
</tr>
<tr>
<td>60 – 90 kg</td>
<td>1500</td>
</tr>
<tr>
<td>&gt; 90kg</td>
<td>2000</td>
</tr>
</tbody>
</table>

**Maintenance dose**

Maintenance dose guidelines based on estimated creatinine clearance (Cockcroft and Gault). See Interval column for the time after the Loading Dose that this should be given:

<table>
<thead>
<tr>
<th>CrCl (ml/min/1.73m²)</th>
<th>Dose (milligrams)</th>
<th>Interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 29 / dialysis</td>
<td>1000</td>
<td>Infrequent</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>(see below)</em></td>
</tr>
<tr>
<td>30 – 39</td>
<td>750</td>
<td>24</td>
</tr>
<tr>
<td>40 – 54</td>
<td>500</td>
<td>12</td>
</tr>
<tr>
<td>55 – 74</td>
<td>750</td>
<td>12</td>
</tr>
<tr>
<td>75 – 89</td>
<td>1000</td>
<td>12</td>
</tr>
<tr>
<td>90 – 110</td>
<td>1250</td>
<td>12</td>
</tr>
<tr>
<td>≥ 111</td>
<td>1500</td>
<td>12</td>
</tr>
</tbody>
</table>

**Cockcroft and Gault equation:**

This is the preferred method for estimating renal function for drug dosing. eGFR should not be routinely used for this purpose.

\[
\text{CrCl(mls/min)} = \frac{(140-\text{age}) \times \text{(weight (kg))} \times \text{Constant}}{\text{SrCreatinine (umol/L)}}
\]

Where Constant is 1.23 for males and 1.04 for females.

*See [Appendix 1](#) for determination of weight for the calculation.

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**6. Roles and responsibilities**

All clinical staff involved in the prescribing of antimicrobials to adhere to this policy including full documentation on EPMAR as detailed.
7. Monitoring document effectiveness

Key standards:

- Document the Indication/rationale for antimicrobial therapy.
- Review and document the patient’s allergy status.
- Ensure the choice of antibiotic complies with the antibiotic guidelines.
- Prescribe single dose antibiotics for surgical prophylaxis, unless policy states otherwise.
- Administer antibiotic prophylaxis within 60 minutes prior to surgical incision (administration must be complete before the incision, and before inflation of the tourniquet when used)

Audits of compliance with the guideline will be conducted on a regular basis as part of the Antibiotic Point Prevalence study. Compliance with guidelines is also one of the elements of the Antibiotic prescribing bundle which is audited monthly.

8. Abbreviations and definitions

BNF – British National Formulary
EPMAR – Electronic prescribing medication administration record
IV - Intravenous
MHRA - Medicines and Healthcare products Regulatory Agency
PO - oral
SPC – Summary of Product Characteristics

9. References

10. Appendices

Appendix 1: Body weight for dose calculation

Body Weight for Calculation

Creatinine production is dependent on muscle mass and therefore, in general, the use of Ideal Body Weight (IBW) is preferred for the Cockcroft and Gault equation.

If the patient's Actual Body weight (ABW) is not far from the IBW (within 120%), or if they are underweight, then the ABW is used for the calculation.

If the patient is obese (>120% IBW), their muscle mass is likely to be larger than predicted when using height in the IBW calculation. An adjusted body weight or even the ABW (e.g. if patient is a body builder) should give the most accurate calculation of renal function, however if the patient is extremely sedentary and has very little additional muscle mass associated with the adiposity, then the IBW would be the most accurate measurement to use.

Due to the complexity of this issue and the risk of overestimating renal function if a higher than necessary weight is used for the calculation, the vancomycin dose calculator will use a maximum weight of 120% of IBW for calculating the creatinine clearance of obese patients. In cases where the muscle mass is believed to be greater than this, the dose should be discussed with a pharmacist.

IBW calculation³:

IBW males = 50kg +[0.9(Height (cm) -152)]

and

IBW females = 45.5kg +[0.9(Height (cm) -152)]

For patients less than 152cm, the weight should be decreased more conservatively. There are no published guidelines on how this should be done. If we were to subtract 0.9kg for every cm under 152cm, the IBW would give the patient a BMI of 18 or less which is classed as underweight.

If you divide the baseline weight of 45.5kg or 50kg for a woman or man (respectively) by 152cm, you will end up with 0.29 kg/cm or 0.32 kg/cm. Taking 0.3kg off for every cm under 5ft, will give a weight that is within the BMI range for that height. For this reason, the equation used in the calculator for patients less than 152cm is:

IBW males = 50kg – [0.3 x (152cm – height)]

and

IBW females = 45.5kg – [0.3 x (152cm – height)]
11. Document Control Information

All sections must be completed by the author prior to submission for approval

<table>
<thead>
<tr>
<th>Lead Author:</th>
<th>Sue Wei Chong Antimicrobial Pharmacist</th>
</tr>
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<tbody>
<tr>
<td>Lead author contact details:</td>
<td><a href="mailto:Suewei.chong@srf.t.nhs.uk">Suewei.chong@srf.t.nhs.uk</a> 01612 065819</td>
</tr>
<tr>
<td>Consultation</td>
<td>Name of person or group</td>
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<td></td>
<td>Antibiotic Steering Group</td>
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<td>Microbiologists</td>
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<td>Respiratory consultants</td>
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<tr>
<td></td>
<td>Dr Elizabeth Trautt</td>
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<td>Dr Alex Peel</td>
</tr>
<tr>
<td>Keywords / phrases:</td>
<td>Antibiotic, infection, vancomycin, TDM</td>
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<td>Communication plan:</td>
<td>The guideline will form part of the Trust Antibiotic Policy and thus can be accessed via the Antibiotic and Infection Control hotlinks area on the front page of Synapse.</td>
</tr>
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<td></td>
<td>In addition, adherence to the policy will be encouraged through FY1 and FY2 teaching sessions.</td>
</tr>
<tr>
<td>Document review arrangements:</td>
<td>This document will be reviewed by the author, or a nominated person, at least once every three years or earlier should a change in legislation, best practice or other change in circumstance dictate.</td>
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This section will be completed following committee approval

<table>
<thead>
<tr>
<th>Guideline Approval:</th>
<th>Name of Approving Committee: Medicines Management Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Chairperson: Richard Cooper</td>
</tr>
<tr>
<td></td>
<td>Approval date: 02/07/2020</td>
</tr>
<tr>
<td></td>
<td>Formal Committee decision</td>
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</table>
**12. Equality Impact Assessment (EqIA) screening tool**

Legislation requires that our documents consider the potential to affect groups differently, and eliminate or minimise this where possible. This process helps to reduce health inequalities by identifying where steps can be taken to ensure the same access, experience and outcomes are achieved across all groups of people. This may require you to do things differently for some groups to reduce any potential differences.

1a) Have you undertaken any consultation/involvement with service users, staff or other groups in relation to this document?  
Yes  
Please state: Discussed at ASG and circulated to microbiologists

1b) Have any amendments been made as a result?  
Yes  
Please Comment: Additional guidance provided on what to do if high or low target levels occur

2) Does this guideline have the potential to affect any of the groups below differently or negatively? This may be linked to access, how the process/procedure is experienced, and/or intended outcomes. Prompts for consideration are provided, but are not an exhaustive list.

<table>
<thead>
<tr>
<th>Protected Group</th>
<th>Yes</th>
<th>No</th>
<th>Unsure</th>
<th>Reasons for decision</th>
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<tr>
<td>Age (e.g. are specific age groups excluded? Would the same process affect age groups in different ways?)</td>
<td></td>
<td></td>
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<tr>
<td>Sex (e.g. is gender neutral language used in the way the guideline or information leaflet is written?)</td>
<td></td>
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<td>X</td>
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<tr>
<td>Race (e.g. any specific needs identified for certain groups such as dress, diet, individual care needs? Are interpretation and translation services required and do staff know how to book these?)</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Religion &amp; Belief (e.g. Jehovah Witness stance on blood transfusions; dietary needs that may conflict with medication offered.)</td>
<td></td>
<td></td>
<td>X</td>
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<tr>
<td>Sexual orientation (e.g. is inclusive language used? Are there different access/prevalence rates?)</td>
<td></td>
<td></td>
<td>X</td>
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<tr>
<td>Pregnancy &amp; Maternity (e.g. are procedures suitable for pregnant and/or breastfeeding women?)</td>
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<tr>
<td>Marital status/civil partnership (e.g. would there be any difference because the individual is/is not married/in a civil partnership?)</td>
<td></td>
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<td>X</td>
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<tr>
<td>Gender Reassignment (e.g. are there particular tests related to gender? Is confidentiality of the patient or staff member maintained?)</td>
<td></td>
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<td>X</td>
<td></td>
</tr>
<tr>
<td>Human Rights (e.g. does it uphold the principles of Fairness, Respect, Equality, Dignity and Autonomy?)</td>
<td></td>
<td></td>
<td>X</td>
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</tr>
<tr>
<td>Carers (e.g. is sufficient notice built in so can take time off work to attend appointment?)</td>
<td></td>
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<td>X</td>
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<tr>
<td>Socio/economic (e.g. would there be any requirement or expectation that may not be able to be met by those on low or unrestricted income?)</td>
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<td>X</td>
<td></td>
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</tbody>
</table>
It is your responsibility to check on the intranet that this printed copy is the latest version.

| **Disability** (e.g. are information/questionnaires/consent forms available in different formats upon request? Are waiting areas suitable?) Includes hearing and/or visual impairments, physical disability, neurodevelopmental impairments e.g. autism, mental health conditions, and long term conditions e.g. cancer. | X |

| Are there any adjustments that need to be made to ensure that people with disabilities have the same access to and outcomes from the service or employment activities as those without disabilities? (e.g. allow extra time for appointments, allow advocates to be present in the room, having access to visual aids, removing requirement to wait in unsuitable environments, etc.) | X |

| 3) Where you have identified that there are potential differences, what steps have you taken to mitigate these? | Not applicable |

| 4) Where you have identified adjustments would need to be made for those with disabilities, what action has been taken? | Not applicable |

| 5) Where the policy, procedure, guidelines, patient information leaflet or project impacts on patients how have you ensured that you have met the Accessible Information Standard – please state below: | ……………………………………………………………………………………………………………………………………………………………………………………………………… |

**EDI Team/Champion only:** does the above ensure compliance with Accessible Information Standard
- Yes
- No

If no what additional mitigation is required:

**Will this guideline require a full impact assessment?** No

**Please state your rationale for the decision:** Minor update to existing guideline which affects all groups in the same way

*(a full impact assessment will be required if you are unsure of the potential to affect a group differently, or if you believe there is a potential for it to affect a group differently and do not know how to mitigate against this - Please contact the Inclusion and Equality team for advice on equality@pat.nhs.uk)*

**Author:** Sue Wei Chong  
**Date:** 1 July 2020

**Sign off from Equality Champion:**  
**Date:**