Clinical Guideline
Clinical Practice Guideline for Dosing and Monitoring of Vancomycin in Adults

Objective file number: 2016-03304
Policy developed by: South Australian expert Advisory Group on Antibiotic Resistance (SAAGAR)

Approved by SA Health Safety & Quality Strategic Governance Committee on: 6 December 2016
Next review due: 6 December 2018

Summary
This guideline provides statewide directive on the safe and effective use of vancomycin in adults.

Keywords
vancomycin, antibiotics, antimicrobial, dosing, monitoring, adults, glycopeptides, therapy, clinical, guideline

Policy history
Is this a new policy? Y
Does this policy amend or update an existing policy? N
Does this policy replace an existing policy? N
If so, which policies?

Applies to All SA Health Portfolio

Staff impact All Clinical, Medical, Nursing, Emergency, Dental, Mental Health, Pathology

PDS reference CG251

Version control and change history

<table>
<thead>
<tr>
<th>Version</th>
<th>Date from</th>
<th>Date to</th>
<th>Amendment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>6/12/2016</td>
<td>6/12/2018</td>
<td>Original version</td>
</tr>
</tbody>
</table>

© Department for Health and Ageing, Government of South Australia. All rights reserved.
Disclaimer
This guideline provides advice of a general nature. This statewide guideline has been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. The guideline is based on a review of published evidence and expert opinion.

Information in this statewide guideline is current at the time of publication.

SA Health does not accept responsibility for the quality or accuracy of material on websites linked from this site and does not sponsor, approve or endorse materials on such links.

Health practitioners in the South Australian public health sector are expected to review specific details of each patient and professionally assess the applicability of the relevant guideline to that clinical situation.

If for good clinical reasons, a decision is made to depart from the guideline, the responsible clinician must document in the patient’s medical record, the decision made, by whom and detailed reasons for the departure from the guideline.

This statewide guideline does not address all the elements of clinical practice and assumes that the individual clinicians are responsible for:

- discussing care with consumers in an environment that is culturally appropriate and which enables respectful confidential discussion. This includes the use of interpreter services where necessary,
- advising consumers of their choice and ensure informed consent is obtained.
- providing care within scope of practice, meeting all legislative requirements and maintaining standards of professional conduct and
- documenting all care in accordance with mandatory and local requirements.

Document title: Clinical Practice Guideline for Dosing and Monitoring of Vancomycin in Adults
First developed: September 2016
Version Number: 1.0
ISBN number: 978-1-74243-846-7
Author: South Australian expert Advisory Group on Antimicrobial Resistance (SAAGAR)
Audience: Medical, nursing, midwifery and allied health staff in South Australia public and private services
Endorsed by: SA Health Safety & Quality Strategic Governance Committee
Contact: 1300 232 272
## Contents

Introduction ............................................................................................................................................ 4  
Background ............................................................................................................................................ 4  
Definitions and acronyms ...................................................................................................................... 4  
Standards .............................................................................................................................................. 5  
Principles of the standards .................................................................................................................... 5  
Loading dose ......................................................................................................................................... 5  
Maintenance dose and dose adjustments ............................................................................................. 6  
Frequency of monitoring and dose adjustment ..................................................................................... 6  
Target therapeutic range ....................................................................................................................... 7  
Administration ........................................................................................................................................ 7  
  Special Considerations ......................................................................................................................... 8  
  Continuous infusions .......................................................................................................................... 8  
  Red man syndrome ........................................................................................................................... 8  
  Obesity ............................................................................................................................................... 8  
Low body weight <50kg ......................................................................................................................... 8  
References ............................................................................................................................................ 9
Introduction

Vancomycin is a glycopeptide antibiotic. Intravenous formulations are used to treat infections with Gram-positive bacteria and for surgical prophylaxis in some situations.

The SA Medicines Formulary restricts use of vancomycin to the following indications:

> Infectious Diseases / Clinical Microbiology advice; or
> Intensive Care Units; or
> Haematology / Oncology as per febrile neutropenia guidelines; or
> Surgical prophylaxis as per statewide clinical guidelines for patients allergic to penicillin or at high risk of methicillin resistant Staphylococcus aureus (MRSA) infection; or
> Continuous Ambulatory Peritoneal Dialysis (CAPD) peritonitis involving methicillin resistant Staphylococcus aureus (MRSA) and coagulase-negative staphylococcus (CoNS); or
> Empiric treatment of sepsis for 48 hours only (continuing therapy only with ID / Microbiology advice).

Note: The dosing recommendations in this guideline are not to be used for treatment of bacterial meningitis. For alternative dosing, consult Infectious Diseases or Clinical Microbiology specialists.

Background

Therapeutic drug monitoring is recommended for all patients treated with vancomycin for longer than 48 hours to avoid under-dosing. Monitoring is also important to minimise the risk of toxicity, especially in patients with renal impairment (including those receiving renal replacement therapy).

Recent evidence has shown that the best determinant of vancomycin efficacy is the AUC/MIC \[1\]. A 24-hour AUC/MIC of 400 or more is the target for clinical success \[2\]. For practical reasons, a trough (pre-dose) plasma concentration is used as a surrogate measure of efficacy.

Definitions and acronyms

**ABW** means: actual body weight

**AUC/MIC** means: ratio of area under the curve (plasma concentration vs time) to minimum inhibitory concentration (Units are mg.hr/Litre)

**BMI** means: body mass index – Estimate of BMI = \((\text{Bodyweight in kilograms}) / (\text{height in meters})^2\)

**BSI** means: blood stream infection/s

**CAPD** means: continuous ambulatory peritoneal dialysis

**CNS** means: central nervous system

**GFR** means: glomerular filtration rate

**ID** means: infectious diseases

**Low weight** means: body weight < 50kg

**MIC** means: minimum inhibitory concentration

**MRSA** means: methicillin resistant Staphylococcus aureus

**NSQHS** means: National Safety and Quality Health Service Standards

**Obese** means: BMI > 30kg/m\(^2\)
SAAGAR means: South Australian SA expert Advisory Group on Antimicrobial Resistance (SAAGAR)
SBP means: systolic blood pressure
TDM means: therapeutic drug monitoring
Trough level means: a serum vancomycin level taken at the end of the dosing interval, approximately one hour prior to next dose

**Standards**

The following National Safety and Quality Health Service Standard (NSQHSS) standards apply:

**Standard 3 – Preventing & Controlling Healthcare Associated Infections**

> Criterion 3.14 – Developing, implementing and regularly reviewing the effectiveness of the antimicrobial stewardship system.

**Standard 4 – Medication Safety**

> Criterion 4.1 – Developing and implementing governance arrangements and organisational policies, procedures and/or protocols for medication safety, which are consistent with national and jurisdictional legislative requirements, policies and guidelines.

**Principles of the standards**

Standard 3 aims to prevent patients from acquiring preventable healthcare associated infections and effectively manage infections when they occur by using evidence-based strategies that are based on the risk to both patients and staff.

Standard 4 aims to ensure competent clinician safely prescribe, dispense and administer appropriate medicines to informed patients and carers.

**Loading dose**

Based on the currently available evidence, clinical data support a loading dose of **25mg / kg (actual body weight)** [2]. A loading dose will facilitate more rapid attainment of therapeutic target range [3].

Table 1: Loading dose determination

<table>
<thead>
<tr>
<th>Actual body weight (kg)</th>
<th>Loading dose (grams)</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-44kg</td>
<td>1g</td>
</tr>
<tr>
<td>45-54kg</td>
<td>1.25g</td>
</tr>
<tr>
<td>55-64kg</td>
<td>1.5g</td>
</tr>
<tr>
<td>65-79kg</td>
<td>2g</td>
</tr>
<tr>
<td>80-119kg or ≥120kg &amp; GFR &lt; 59ml/min</td>
<td>2.5g</td>
</tr>
<tr>
<td>≥120kg and GFR ≥60ml/min</td>
<td>3g* (maximum)</td>
</tr>
</tbody>
</table>

* High loading doses recommended based on expert advice and current practice in Australian and evidence of safety [4-6].
Maintenance dose and dose adjustments

Table 2 below presents suggested maintenance dosing for patients within weight range between 50 & 120 kg. Outside of this range, dosing based on actual body weight at 15 mg/kg per dose may be indicated (see guide on dosing in obesity or low body weight below).

Commence maintenance dosing approximately 12 hours after loading dose if GFR ≥ 40mL/min, OR 24 hours after loading dose if GFR = 20-39 mL/min. If GFR < 20mL/min check trough level 24 hours after loading dose; wait for trough result prior to re-dosing.

Table 2: Maintenance dose determination

<table>
<thead>
<tr>
<th>GFR (mL/min)#</th>
<th>GFR &gt;90</th>
<th>GFR 60-90</th>
<th>GFR 40-59</th>
<th>GFR 20-39</th>
<th>GFR &lt;20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maintenance dose</td>
<td>1.5g 12-hourly</td>
<td>1g 12-hourly</td>
<td>750mg 12-hourly</td>
<td>1g 24-hourly</td>
<td>1g every 2 to 7 days</td>
</tr>
</tbody>
</table>

**Dosage Adjustment (intermittent infusions)**

- **Trough level < 10mg/L**: Convert to 1g 6-hourly.
- **Trough level 10 – 14.9 mg/L**: Convert to 1.25g 8-hourly.
- **Trough level 15 – 20mg/L**: IN TARGET RANGE - no change required. Repeat trough levels twice weekly if vancomycin levels and renal function are stable. If not, more frequent monitoring is suggested*
- **Trough level 21 – 25mg/L**: Convert to 1.25g 12-hourly, Convert to 750mg 12-hourly.
- **Trough level > 25mg/L**: Convert to 1g 12-hourly, Monitor 48-hourly, Re-dose when trough <20mg/L.

**Trough level > 30mg/L**

- Hold dose for 24 hours. Re-check level and recommence at reduced dose when level < 20mg/L. Review renal function

* Expert opinion, for further advice consult pharmacist; † Magnitude of dose increase dependent of trough level & GFR. Consider change to continuous infusion.# Use a GFR calculator if available on-line at your site. eGFR is a suitable estimate for adult patients with stable renal function who are neither obese or underweight.

Frequency of monitoring and dose adjustment

The time of the first TDM (trough) will depend on the patient’s renal function and/or if renal function is potentially unstable.

For patients with normal renal function, the first TDM (trough) should occur just prior (within one hour) to the fourth dose or on day 3, whichever occurs earlier. In patients with GFR between 20-39 mL/min check trough level before (within one hour) of the third dose. In changing renal function, earlier or more frequent TDM may be required. For patients with GFR < 20mL/min or on peritoneal dialysis check trough level 24- hours after loading dose. Repeat TDM trough (pre-dose) level every 3 days until levels are stable within the therapeutic range, and at least once weekly thereafter [7, 8].

Measure serum creatinine twice weekly. Unless stated in the table above, doses should NOT be routinely withheld pending trough level result.

For patients with unstable renal function TDM should occur more frequently (possibly daily) to ensure toxicity is avoided. Creatinine levels should be checked daily for the first 2 to 3 days of therapy, even if creatinine levels are in the normal range.
Target therapeutic range

Intermittent infusion: 15 - 20mg/L; continuous infusion: 20 - 25mg/L. Clinicians may aim for targets of 20 - 25mg/L particularly for CNS infections [2] – for further information seek advice from Infectious Diseases / Clinical Microbiology/ Clinical Pharmacist.

Administration

Doses of 1g should be administered over at least 60 minutes. For higher doses the duration of infusion should be extended by 30 minutes for each additional 500mg. This is recommended to reduce the risk of red man syndrome [8, 9]. The usual dilution is 5mg/mL; for fluid-restricted patients, concentrations of up to 10mg/mL may be used [10].

Minimum infusion durations are shown in the table below adapted from Wilson, 2011 [11].

Table 3: Intravenous administration

<table>
<thead>
<tr>
<th>Dose</th>
<th>Minimum Infusion Duration*</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 1 g</td>
<td>60 min</td>
</tr>
<tr>
<td>1.1 - 1.5 g</td>
<td>90 min</td>
</tr>
<tr>
<td>1.6 - 2.0 g</td>
<td>120 min</td>
</tr>
<tr>
<td>&gt; 2 g</td>
<td>Infuse at approx. 1 g per hour</td>
</tr>
</tbody>
</table>

* In some instances, it may be appropriate to infuse more rapidly if the patient can tolerate it.
Special Considerations

Continuous infusions

Continuous infusion of vancomycin may be useful in patients where the target range is difficult to achieve via intermittent infusion, and may be necessary to maintain adequate blood levels in patients with augmented renal function or medically obese patients. Continuous infusions may limit the increased risk of nephrotoxicity observed with administration of high doses of vancomycin observed with intermittent infusions [12].

The conversion dose when switching to a 24 hour continuous infusion is nominally the same as the total dose for 24 hours administered via intermittent confusion [2]. For patients being discharged and continuing treatment at home, and with levels in the target range, local experts from SAAGAR recommend a dose reduction of approximately 20% when converting from intermittent to 24-hour continuous infusion.

During continuous infusions blood may be drawn at any time after 24 hours of therapy to obtain an accurate level, and potentially sooner if a loading dose is used [13]. Dosage adjustments are made in a simple linear manner [2].

Red man syndrome

Red man syndrome is a non-immunological reaction that can occur during or shortly after an infusion of vancomycin and is related to the rate of infusion. The reaction is mediated by histamine release, which can result in pruritus, flushing, erythematous rash (face, neck and upper thorax predominantly), fever, chills and in severe cases angioedema and hypotension. These symptoms are due to non-specific mast cell degranulation. True IgE-mediated allergy can occur but is rare.

If a patient experiences an infusion related reaction to vancomycin:
1. Cease infusion
2. Administer antihistamine (cetirizine 10mg PO)
3. If newly hypotensive (SBP<90mmHg) initiate a MET call. Consider giving adrenaline if unable to do so.
4. Consult clinical pharmacist or Infectious Diseases team for advice on recommencement of vancomycin at a slower rate of infusion. Local experts from SA recommend doubling the time to infuse the solution, or changing to a continuous infusion.

Obesity

The volume of distribution is larger and clearance of vancomycin greater in the obese population. Weight-based dosing using actual body weight (15mg/kg 12-hourly if GFR ≥40mL/min, maximum 2 grams per dose) is recommended [11]. More frequent dosing (8-hourly) or a continuous infusion may be suitable in obese patients [14]. Higher doses of more than 4g per day, such as those often required in obese patients, are associated with a higher risk of nephrotoxicity [15, 16].

Low body weight <50kg

Consider 15mg/kg 12-hourly maintenance dosing for patients <55kg, appropriately adjusting the dose if the patient also has impaired renal function. Loading doses less than 25mg/kg and less frequent dosing may be appropriate in these patients [17].
References


For more information

National Antimicrobial Utilisation Surveillance Program
Communicable Disease Control Branch
11 Hindmarsh Square
Adelaide SA 5000
Telephone: 1300 232 272
Email: HealthAntibio@sa.gov.au
www.sahealth.sa.gov.au/antimicrobials

Public-11-A2

© Department for Health and Ageing, Government of South Australia. All rights reserved