GUIDELINES FOR VANCOMYCIN DOSING AND MONITORING IN ADULT PATIENTS

This guidance does not override the individual responsibility of health professionals to make appropriate decision according to the circumstances of the individual patient in consultation with the patient and /or carer. Health care professionals must be prepared to justify any deviation from this guidance.

Introduction

This guideline covers the prescribing and monitoring of vancomycin for all adult patients.

This guideline is for use by the following staff groups:

All qualified healthcare professionals involved in prescribing, administering or monitoring glycopeptide antibiotics.

Lead Clinician(s)

Keith Hinton	Lead Pharmacist Critical Care, Theatres and Surgery
Approved by Accountable Director Steve Graystone on:	22nd January 2014
Extension approved by TMC on:	November 2017
Review Date: This is the most current document and is to be used until a revised version is available	6th February 2021

Key amendments to this document:

Date	Amendment	By:
05.01.2011	No amendments made to guideline	K Hinton
26.01.2012	No amendments made to guideline	K Hinton
14.11.2012	Amendment made to target plasma concentration and dosage. Additional information included regarding infusion related side effects	K Hinton
21.1.2014	Reformatted to improve clarity of information	K Hinton
31.03.2016	Document extended for 12 months as per TMC paper approved on 22nd July 2015	TMC
02/09/2017	Document extended for 3 months, no changes made, awaiting approval	K Hinton
08/06/2017	Document extended for 3 months, to allow for incorporation of new calculator	K Hinton
August 2017	Document extended for 3 months as per TMC paper approved 22nd July 2015	TMC
November 2017	Document extended for three months whilst under review	TLG
December 2017	Sentence added in at the request of the Coroner	
March 2018	Document extended for 3 months as approved by TLG	TLG
June 2018	Document extended for 3 months as approved by TLG	TLG
February 2019	Removal of link to creatinine clearance calculator (no longer available)	K Hinton

GUIDELINES FOR VANCOMYCIN DOSING AND MONITORING IN ADULT PATIENTS

Introduction to Vancomycin Therapy (BNF Section 5.1.7)

The glycopeptide antibiotic vancomycin has bactericidal activity against aerobic and anaerobic Gram-positive bacteria including multi-resistant staphylococci, although there have been reports of glycopeptide resistant *Staph. aureus* and enterococci [1, 2].

Glycopeptides are not absorbed from the gut and must therefore be given by injection for systemic infections. They are potentially toxic, so appropriate dosing (and for vancomycin, routine serum monitoring) is important to avoid both excessive and sub-therapeutic concentrations, thus preventing toxicity and ensuring efficacy. Vancomycin is the first-line choice in WAHT

Vancomycin dosage

- Calculate the patient's renal function using the equation below.
- Patients with good renal function (creatinine clearance ≥90ml/minute) should receive a dose of 15mg/kg twice a day[1] (rounded to the nearest 250mg)

Patient actual body weight	Suggested vancomycin dose in good renal function (creatinine clearance ≥90ml/minute)
< 50kg	750mg BD
50-75kg	1000mg BD
76-90kg	1250mg BD
>90kg	1500mg BD

In stable renal function, calculate patient's creatinine clearance using the Cockcroft-Gault equations[2]

Men: $CrCl = \frac{1.23 \times (140 - age) \times weight\ (kg)}{Serum\ creatinine\ (micromol/l)}$

Women: $CrCl = \frac{1.04 \times (140 - age) \times weight\ (kg)}{Serum\ creatinine\ (micromol/l)}$

If patient is obese (i.e. >20% above ideal body weight) calculate creatinine clearance using ideal body weight (IBW) using:

Men (IBW): 50kg + (2.3kg x number of inches over 5foot or 2.5cm above 152cm)

Women (IBW): 45kg + (2.3kg x number of inches over 5foot or 2.5cm above 152cm)

The BNF[3] recommends reducing the dose in patients over the age of 65 years. In contrast, this guidance recommends dosage based on patients weight and renal function (where age is a contributing factor).

Vancomycin dosage in renal impairment

Creatinine clearance CrCl (ml/min)	Recommended IV dosage	Timing of initial trough (pre-dose) level
51-89	1g BD (750mg BD in patients ≤50kg)	Prior to 3rd or 4th dose (preferably morning dose)
20-50	500mg BD	Prior to 2nd or 3rd dose
< 20	Single dose of 1g only and seek advice from Microbiology	Seek advice from Microbiology

In acute renal dysfunction, discuss the appropriateness of vancomycin therapy with the microbiologist. If vancomycin therapy is appropriate, use a dose of 1g and check plasma concentration 24 hours after dose given. Repeat assays daily until plasma level is <20mg/L. Do not give a further dose unless concentration is <20mg/L.

Administration [4, 5] **:**

- Reconstitute each: 500mg vial with 10ml water for injection (50mg/ml)
  1g vial with 20ml water for injection (50mg/ml)
- Administer by intravenous infusion in sodium chloride 0.9% or glucose 5%
- Infuse at a **maximum rate of 10mg/minute** (e.g. 1g over at least 100 minutes) to avoid rapid infusion related adverse effects e.g. flushing (red man syndrome) hypotension and shock. If side effects are experienced, stop the infusion and seek advice. In most instances vancomycin therapy may be continued but infused at a slower rate.

Dose	Volume of solution	Minimum infusion duration	Maximum infusion rate
1000mg	250ml	100 minutes	150ml/hour
750mg	250ml	75 minutes	200ml/hour
500mg	100ml	60 minutes	100ml/hour

Vancomycin monitoring:

- Monitoring required is trough (pre-dose) concentration only
- Target concentration is 10-20mg/l.
- Higher levels (15-20mg/l) may be required in specific situations as directed by the microbiologist.
- Oral vancomycin therapy for Clostridium difficile and once only injections do **not** require blood concentration monitoring.

If on regular dosage:

measure first **trough level** as described in table. Continue dosage regime if concentration is 10-20mg/l. Concentrations outside this range may require adjustment of dosage +/- dosage interval (discuss with ward/on-call pharmacist or Microbiologist)

- If renal function is stable (e.g. patient has good urine output) continue with the dosage regimen until the plasma level is obtained i.e. **do not omit a dose whilst awaiting the result.**

If in established renal failure (creatinine clearance <20ml/minute):

Follow the guidance in the table above. Repeat assays daily until plasma level is <20mg/L. Do not give a further dose unless concentration is <20mg/L

- Check U+Es regularly whilst the patient is on IV vancomycin e.g. daily when starting therapy and less frequently when renal function is stable on long term therapy.

Information required on the request form:

- patient details
- drug given, dose and dosage interval
- time last dose given
- time blood sample taken (trough or random)

Interpretation and dosage adjustment

For most indications, the target trough (pre-dose) concentration is 10–20 mg/L. Higher levels may be required in serious infections e.g. bacteraemia, endocarditis and osteomyelitis, which will be advised by the Consultant Microbiologist.

The vancomycin trough (pre-dose) concentration will indicate further action(s) to be taken:

Trough (pre-dose) level	Interpretation	Action(s) required
< 10mg/L	**Too low**	Increase daily vancomycin dose (see table below)
10 – 14.9mg/L	Low if serious infection	Serious infection → increase daily vancomycin dose (see table below) Non-serious infection → continue same dosing regimen and re-check level in 24 hours.
10 – 20mg/L *or* 15-20mg/l *in serious infection*	**Good**	Continue same treatment regimen.
>20 mg/L	**Too high**	Withhold further vancomycin therapy and discuss therapeutic options with Consultant Microbiologist. If vancomycin therapy is to be continued, reduce dose (see table below) and resume therapy once level is <20mg/L. Re-check level 24 hours later.

Please note that increments and reductions should be rounded up or down to the nearest 250mg with the lowest practical single dose is 500mg. The following table is intended as a guide of dose adjustments. For dosing advice contact the microbiologist or your ward Pharmacist / Medicines Information helpline (ext 30235) or the on-call pharmacist (out of hours via switchboard)

Dosing regimen	Increment required	Reduction required
1000mg 12 hourly	1250mg 12 hourly or 1500mg 12 hourly if level <10mg/l	750mg 12 hourly
750mg 12 hourly	1000mg 12 hourly	1000mg 24 hourly
1000mg 24 hourly	750mg 12 hourly	Seek advice

Further vancomycin monitoring:

Patient	Monitoring Frequency
Stable renal function, vancomycin level is within target range	Re-check every 3-4 days
Fluctuating renal function e.g. reduction in urine output	Every 24 hours
Concomitant nephrotoxic therapy (e.g. amphotericin, gentamicin, tobramycin, iv contrast)	Every 24 hours

Monitoring Tool

Following the introduction of this guideline an audit will be carried out within one year by Pharmacy/Microbiology to monitor compliance

STANDARDS	%	CLINICAL EXCEPTIONS
All prescriptions for vancomycin will be prescribed and monitored according to this guideline	100	

References

1. Mohammedi I. et al. Loading dose of vancomycin in critically ill patients: 15mg/kg is a better choice than 500mg. International Journal of Antimicrobial Agents. Vol. 27 (3) March 2006; 259-262

2. Cockcroft D, Gault MD. Nephron, 16:31-41, 1976

3. British Medical Association and the Royal Pharmaceutical Society (2013). The British National Formulary. 66th ed. London: BMJ Group and Pharmaceutical Press.

4. Wockhardt UK Ltd. Summary of Product Characteristics [Internet]. Vancomycin 1g powder for solution for infusion. November 2012. [Accessed 20/1/2014] |Available from: www.emc.medicines.org.uk

5. Hospira UK Ltd. Summary of Product Characteristics [Internet]. Vancomycin hydrochloride 500mg and 1g powder for concentrate for infusion. January 2009. [Accessed 20/1/2014] |Available from: www.emc.medicines.org.uk

6. Therapeutic Monitoring of Vancomycin in Adult Patients: A Consensus Review of the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, and the Society of Infectious Diseases Pharmacists. Am J Health-Syst Pharm. 2009; 66:82–98.

7. Gould F.K, Denning D.W, Elliott T.S.J, Foweraker J, Perry J.D, Prendergast B.D, Sandoe J.A.T, Spry M.J and Watkin R.W (2012). Guidelines for the diagnosis and antibiotic treatment of endocarditis in adults: a report of the Working Party of the British Society for Antimicrobial Chemotherapy. Journal of Antimicrobial Chemotherapy 67 (2) pp 269-289.

CONTRIBUTION LIST

Key individuals involved in developing the document

Name	Designation
Keith Hinton	Lead Pharmacist Critical Care, Theatres and Surgery

Circulated to the following individuals for comments

Name	Designation
Rachael Montgomery	Chief Clinical Pharmacist WAHT

Circulated to the chair of the following committee's / groups for comments

Name	Committee / group

Supporting Document 1 - Equality Impact Assessment Tool

To be completed by the key document author and attached to key document when submitted to the appropriate committee for consideration and approval.

		Yes/No	Comments
1.	**Does the policy/guidance affect one group less or more favourably than another on the basis of:**		
	• Race	No	
	• Ethnic origins (including gypsies and travellers)	No	
	• Nationality	No	
	• Gender	No	
	• Culture	No	
	• Religion or belief	No	
	• Sexual orientation including lesbian, gay and bisexual people	No	
	• Age	No	
	• Disability	No	
2.	**Is there any evidence that some groups are affected differently?**	No	
3.	**If you have identified potential discrimination, are any exceptions valid, legal and/or justifiable?**	No	
4.	**Is the impact of the policy/guidance likely to be negative?**	No	
5.	**If so can the impact be avoided?**	N/A	
6.	**What alternatives are there to achieving the policy/guidance without the impact?**	N/A	
7.	**Can we reduce the impact by taking different action?**	N/A	

If you have identified a potential discriminatory impact of this key document, please refer it to Human Resources, together with any suggestions as to the action required to avoid/reduce this impact.

For advice in respect of answering the above questions, please contact Human Resources.

Supporting Document 2 – Financial Impact Assessment

To be completed by the key document author and attached to key document when submitted to the appropriate committee for consideration and approval.

	Title of document:	Yes/No
1.	Does the implementation of this document require any additional Capital resources	No
2.	Does the implementation of this document require additional revenue	No
3.	Does the implementation of this document require additional manpower	No
4.	Does the implementation of this document release any manpower costs through a change in practice	No
5.	Are there additional staff training costs associated with implementing this document which cannot be delivered through current training programmes or allocated training times for staff	No
	Other comments:	

If the response to any of the above is yes, please complete a business case and which is signed by your Finance Manager and Directorate Manager for consideration by the Accountable Director before progressing to the relevant committee for approval