Gloucestershire Hospitals NHS

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Policy for the use of intravenous vancomycin in adults (pulsed dose)

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Gloucestershire Hospitals NHS

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TRUST POLICIES

Authorisation Form

DOCUMENT:

Policy for the use of pulsed dose intravenous vancomycin in Adults

Authorisation	Name and Position	Date Approved
Responsible Authors	Dr. Robert Jackson Consultant Microbiologist Delyth Ahearne Antimicrobial Pharmacist	17th May 2017
Policy Sponsor	Dr. Alan Lees Consultant Microbiologist GHNHSFT Antimicrobial Stewardship Lead	17th May 2017
Assured by	Antimicrobial Stewardship Committee	17th May 2017

Consideration at authorised groups (e.g. Board, Board sub committees, Policy Group, Clinical policies Sub Group, Departmental meetings etc)

Name of Group	Minute details	Date considered
Antimicrobial Stewardship Committee	Considered under Matters Arising 17/5/17	17th May 2017
Sent for consultation to Lead Consultant Intensivist and Lead Consultant Nephrologist	Policy agreed with leads on 17/5/17 – Preetham Boddana, Alex D'agapeyeff and Matt Oram	May 2017

Policy for the use of intravenous vancomycin in adults (pulsed dose)

Objective:

Provide a policy for the administration and monitoring of intravenous vancomycin in adult patients at Gloucestershire Hospitals NHS Foundation Trust (GHNHSFT).

Background/policy statement:

This policy covers the use of intravenous (iv) vancomycin prescribed as an intermittent (pulsed) infusion in adults. Vancomycin is typically administered twice daily.

This policy also includes guidance on use of iv vancomycin in patients with renal impairment receiving renal replacement therapy in departments of critical care (haemofiltration).

Cautions and contraindications:

- Contra-indications to vancomycin therapy – hypersensitivity

Cautions for vancomycin therapy:

- To avoid the risk of “red-man (red neck) syndrome”, pain or muscle spasm, ensure that the administration rate is not faster than 500 mg per hour

- 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 iv vancomycin. Where possible, avoid co-administration with the following:

    - amphotericin
    - potent diuretics
    - aminoglycosides eg gentamicin, tobramycin and amikacin
    - NSAIDs
    - ACE inhibitors

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

- Due to potential ototoxicity, vancomycin should be avoided in patients with previous hearing loss – audiometry may be necessary for monitoring in selected patients

- Vancomycin should be used with caution in patients with **renal impairment**.

Dosage and Prescribing

Prescription of vancomycin should be on the GHNHSFT Drug Chart. The initial **loading dose** should be prescribed in the section for *Once only medications and first dose of antibiotic* (page 1) and **maintenance dose** prescription on the *Anti-infectives* pages. If the vancomycin maintenance dose is adjusted, the maintenance dose prescription must be rewritten with the new dose and a new start date for the altered prescription.

The drug chart can be annotated to show when pre-dose (trough) vancomycin levels are due to be taken – this can be done by writing a box around the dose before which a blood level should be taken. The vancomycin regime should be reviewed in the light of the results of the vancomycin level normally in the interval between when the dose that has just been given and when the subsequent vancomycin dose is due.

Initial dosing should be based on the instructions in **table 1** (loading dose) and **table 2** (maintenance dose). The actual dose and time interval between doses are based on estimated creatinine clearance (see **Box 1**) and actual body weight.

Box 1: Estimation of creatinine clearance (CrCl)

The following 'Cockcroft Gault' equation can be used to estimate creatinine clearance (CrCl)

$$\text{CrCl (mL/min)} = \frac{[140 - \text{age (years)}] \times \text{weight (kg)} \times 1.23 \text{ (male) OR} \times 1.04 \text{ (female)}}{\text{serum creatinine (micromol/L)}}$$

Cautions

- Use **actual body weight** or **maximum body weight***, whichever is lowest
- A current eGFR can be used as an alternative to estimated creatinine clearance

*See Appendix 1 for *maximum body weight table*

Calculating and prescribing the loading dose

Please note that the loading dose is based on actual body weight only and does not take account of renal function. Loading doses are 20 mg/kg with rounding up to the nearest 250 mg. See table 1.

On rare occasions a patient's clearance of vancomycin may be so high that the maintenance dose is higher than the calculated loading dose. In these circumstances, the loading dose should be the higher of the loading and maintenance doses i.e. if loading dose is calculated as lower than maintenance dose then give the maintenance dose as a loading dose instead.

Prescribe the loading dose on the section of the drug chart for *Once only medications and first dose of antibiotic* (page 1).

For maternity sepsis, use ***current actual body weight*** to calculate the loading and maintenance dosage regimen.

Table 1: Initial vancomycin LOADING dose

Actual body weight	Dose	Volume of sodium chloride (0.9%)*	Duration of infusion
< 40 kg	750 mg	250 mL	90 minutes
40 – 59 kg	1000 mg	250 mL	2 hours
60 – 90 kg	1500 mg	500 mL	3 hours
> 90 kg	2000 mg**	500 mL	4 hours

*Glucose 5% may be used in patients with sodium restriction.
**Maximum dose of 1.5 g if creatinine clearance is <30 mL/min

Calculating and prescribing the maintenance dosage regimen

Give the first maintenance infusion 8,12, or 48 hours after the loading dose as per the "Dose Interval" column in Table 2 (below).

Table 2: Vancomycin MAINTENANCE dosage regimen

Vancomycin pulsed (divided daily) dose infusion – initial maintenance dosage guidelines					
CrCl (mL/min)	**Dose**	**Duration of infusion**	**Volume of sodium chloride (0.9%)***	**Dose Interval**	**Timing of first pre-dose vancomycin level**
< 20	500 mg	1 hour	250 mL	48 hours	Pre the 2nd dose
20 - 29	250 mg	1 hour	250 mL	12 hours	Pre the 3rd dose
30 - 39	375 mg	1 hour	250 mL	12 hours	Pre the 3rd dose
40 - 54	500 mg	1 hour	250 mL	12 hours	Pre the 4th dose
55 - 74	750 mg	90 minutes	250 mL	12 hours	Pre the 5th dose
75 - 89	1000 mg	2 hours	250 mL	12 hours	Pre the 5th dose
90 - 110	1250 mg	2 ½ hours	250 mL	12 hours	Pre the 5th dose
>110	1000 mg	2 hours	250 mL	8 hours	Pre the 5th dose

* Glucose 5% may be used in patients with sodium restriction. **Doses greater than 1250mg and up to 2000 mg can be diluted in 500 mL fluid.**

The usual frequency of vancomycin administration is ***twice daily***. Exceptions are if creatinine clearance is >110 and <20 (see table 2.).

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.

Higher concentrations are required in the following conditions:

- Confirmed bacteraemia with a significant Gram positive bacterium
- Endocarditis
- Osteomyelitis

- Meningitis
- Hospital-acquired pneumonia (HAP)
- Ventilator associated pneumonia (VAP)
- Other infections caused by resistant organisms where the responsible organism is sensitive to vancomycin but has a relatively high minimum inhibitory concentration (MIC) – Microbiology will advise in these instances

Monitoring the serum vancomycin concentration levels

Vancomycin levels are performed by CHEMICAL PATHOLOGY. Send requests for vancomycin levels on CHEMICAL PATHOLOGY request forms.

Information on vancomycin levels can be found on the Pathology Intranet pages.

Most vancomycin levels are planned (non-urgent) investigations - samples should ideally not be collected or sent for testing between midnight and 6am, except in exceptional circumstances.

The drug chart can be annotated to show when pre-dose (trough) vancomycin levels are due to be taken – this can be done by writing a box around the dose before which a blood level should be taken.

Only patients on iv vancomycin require monitoring of serum vancomycin levels. On rare occasions it may be necessary to perform vancomycin levels in selected patients receiving high dose oral vancomycin (if they have extensive gut inflammation and/or have impaired renal function). The vast majority of patients being given oral vancomycin (for *Clostridium difficile* infection) do not require monitoring of vancomycin levels.

Blood sample forms must include the following minimum information:

- Date and time of blood sample taken
- Dose and frequency
- Start date of the vancomycin course

Once the patient has been established on the maintenance dosage regimen it is essential to monitor vancomycin levels to ensure these are in the therapeutic and non-toxic range. If the levels are taken correctly and are found to be out of the target range, the initial maintenance dosing regimen will need modifying.

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 the first pre-dose (trough) sample according to the timings recommended in the right hand column of **table 2**.

Frequency of monitoring of vancomycin levels

- every 2 - 3 days if renal function is stable
- daily if the patient has unstable renal function
- Monitor creatinine regularly – frequency of monitoring decided on a case by case basis - daily monitoring if unstable renal function or renal impairment at initiation or during vancomycin therapy

Record the exact time of all vancomycin levels on the sample request form and in the medical

records.
If renal function is stable, give the next dose before the trough result is available. The vancomycin regime should be reviewed in the light of the results of the vancomycin level in the time between when the dose that has just been given and the subsequent vancomycin dose.
If renal function is deteriorating, withhold the next immediate dose until the result is available then follow the advice in **Table 3**.

Monitor the vancomycin concentration levels and reassess the dosage regimen

Target serum vancomycin concentrations:

- Target trough concentration range: 10 – 20 mg/L
- If the patient is seriously ill (severe or deep-seated infections), the target range is 15 – 20 mg/L. If the measured concentration is < 15 mg/L, consider increasing the dose or reducing the dosage interval (see 8 hourly dosing above)
- If the patient is failing to respond, seek advice from duty consultant microbiologist and senior clinician

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, 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?*
    - Was the sample taken post administration (post dose), inadvertently*
    - Has renal function declined or improved?
    - Does the patient have oedema or ascites?

*If any of these are applicable, repeat the pre-dose vancomycin level prior to the next dose to clarify.

If in doubt about the vancomycin levels, repeat the vancomycin level (pre-dose) before modifying the dosage regimen and consider contacting pharmacy for advice.

Table 3: Adjustment of Vancomycin Dosage Regimen

Vancomycin concentration	Suggested dose change or action
<10 mg/L	Was the level taken correctly ? If “yes”, Increase the dose by 50% and consider reducing the dosage interval or seek advice
10 – 15 mg/L	If the patient is responding, maintain the present dosage regimen. If the patient is seriously ill, consider increasing the dose amount or reducing the dosage interval to achieve a trough level of 15 – 20 mg/L.
15 – 20 mg/L	Maintain the present dosage regimen
21-25 mg/L	Reduce the dose by 25% and repeat pre-dose level taken 48 hours after dose change
>25 mg/L	Was the level taken correctly ? If “yes”, **do not administer further vancomycin** until a trough / random level is <20. Then re-prescribe the vancomycin at a lower dose if it is clinically appropriate to continue this antibiotic – seek advice

General points

- Record the exact times of all measured concentrations on the vancomycin request form and in the medical records
- 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
- Review the need for vancomycin daily

Box 2: Toxicity

- Monitor creatinine regularly (daily if significant existing renal impairment or unstable renal function). 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

For further advice or clarification during normal working hours please contact:

☎ Medicines Information:	CGH ext. 3030	GRH ext. 6108
☎ Duty Consultant Microbiologist:	CGH ext. 4430	GRH ext. 5054

Use of iv vancomycin in patients with renal impairment receiving renal replacement therapy – contact the renal team or renal pharmacist

For guidance on intraperitoneal administration of vancomycin in patients receiving peritoneal dialysis see PD Antibiotic guidelines.

Haemofiltration Patients on Departments of Critical Care
The principles for vancomycin dosing and administration are similar to those for patients not on renal replacement therapy. An initial loading dose is given (15 mg/kg) (see table 4) followed by an initial maintenance dose of 1g 48 hours after the loading dose. Regular maintenance doses are given every 48 hours with the dose being adjusted according to pre-dose levels taken prior to the third and all subsequent doses. The results of the pre-dose levels should be reviewed before deciding whether the maintenance dose of 1g requires adjustment. The dose can then be administered.

Table 4: Initial vancomycin LOADING dose – Haemofiltration - DCC

Actual body weight	Loading dose	Volume of sodium chloride (0.9%)*	Duration of infusion
< 50 kg	750 mg	100 mL	75 minutes
51 - 59 kg	750 mg	100 mL	75 minutes
60 - 75 kg	1000 mg	250 mL	100 minutes
76 – 85 kg	1250 mg	250 mL	125 minutes
>85 kg	1500 mg	250 mL	150 minutes

Maintenance dose adjustment for the third dose of vancomycin (second maintenance dose):-

If level < 10 mg/L increase maintenance dose to 1.25 g
If level 10-20 – use maintenance dose of 1g
If level 20-25 – use maintenance dose of 750 mg
If level >25 – omit dose and repeat vancomycin level on the following day (do not give a further dose of vancomycin until the level is <20) – discuss ongoing dose requirement with ward pharmacist or consultant microbiologist.

Selected References:

This policy is based on the Scottish Antimicrobial Prescribing Group (SAPG) Policy for Intravenous Vancomycin Use in Adults Intermittent (Pulsed) Infusion
https://www.scottishmedicines.org.uk/files/sapg/SAPG_Intravenous_vancomycin_adults__Pulsed_infusion_.pdf

SAPG Maximum Body Weight Table
http://www.scottishmedicines.org.uk/files/sapg/Maximum_body_weight_table.pdf

Vancomycin summaries of product characteristics (SPCs) on eMC
http://www.medicines.org.uk/emc/

The Renal Drug Handbook – Caroline Ashley and Aileen Currie (Eds) Radcliffe Publishing Vancomycin – Pages 979-980.

Appendix 1.

Maximum Body Weight Table

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.

Maximum body weight (MBW) table			
Height (feet and inches)	**Height (cm)**	**Male MBW (kg)**	**Female MBW (kg)**
4' 8''	**142**	**49**	**43**
4' 9''	**145**	**52**	**47**
4' 10''	**147**	**54**	**49**
4' 11''	**150**	**58**	**52**
5' 0''	**152**	**60**	**55**
5' 1'	**155**	**62**	**58**
5' 2''	**158**	**66**	**60**
5' 3''	**160**	**68**	**62**
5' 4''	**163**	**71**	**66**
5' 5''	**165**	**74**	**68**
5' 6''	**168**	**77**	**71**
5' 7''	**170**	**79**	**74**
5' 8''	**173**	**82**	**77**
5' 9''	**175**	**85**	**79**
5' 10''	**178**	**88**	**82**
5' 11''	**180**	**90**	**85**
6' 0''	**183**	**94**	**88**
6' 1''	**185**	**96**	**90**
6' 2''	**188**	**98**	**94**
6' 3''	**191**	**101**	**97**
6' 4''	**193**	**104**	**99**
6' 5''	**195**	**107**	**101**
6' 6''	**198**	**109**	**105**
6' 7''	**201**	**113**	**108**
6' 8''	**203**	**115**	**110**