

Intravenous Vancomycin Use in Adults Intermittent (Pulsed) Infusion

Background

This NHS Lanarkshire policy covers the use of intravenous vancomycin prescribed as an intermittent (pulsed) infusion in adult patients ≥ 16 years of age. This can be used for treatment or prophylaxis. Evidence supporting this guidance is detailed below.

Vancomycin can also be prescribed as a continuous infusion. Continuous infusion of vancomycin is preferred, when practical, for patients with severe or deep-seated infections (e.g. pneumonia, endocarditis, bone and joint infections) – refer to separate guidance.

This policy does not apply to the use of vancomycin in patients treated in renal units or receiving haemodialysis or haemofiltration.

Contra-indications and cautions

- ◆ Contra-indications to vancomycin therapy – hypersensitivity
- ◆ Cautions for vancomycin therapy:
 - ◆ To avoid the risk of “red-neck/red-man 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 vancomycin. Where possible, avoid co-administration with the following:
 - ◆ amphotericin
 - ◆ potent diuretics
 - ◆ aminoglycosides
 - ◆ NSAIDs
 - ◆ ACE inhibitors
 - ◆ The above list is not exhaustive – consult the Summary of Product Characteristics SmPC for a full list (www.medicines.org.uk).
 - ◆ In patients with previous hearing loss, use vancomycin with caution or consider alternative antibiotic therapy, due to potential ototoxicity.

Prescribing and documentation

- ◆ To ensure consistency, reduce risk and improve the prescribing of vancomycin, standardised charts (agreed nationally and adopted locally) should be used to document the prescription, administration and monitoring of intermittent vancomycin infusions. These should be used in conjunction with the existing inpatient prescribing chart (e.g. cardex or HEPMA) and medical/nursing documentation.
- ◆ These charts contain a step-wise approach to safe and effective prescribing and key points of advice on monitoring, interpreting and re-prescribing.
- ◆ An Antimicrobial app and an online calculator are available and should be used to calculate the initial dose requirements.

Reference:

A H Thomson et al, Development and evaluation of vancomycin dosage guidelines designed to achieve new target concentrations, J Antimicrob Chemother (2009) 63 (5): 1050-1057.

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STEP 1:

Prescribe the loading dose and maintenance dosage regimen

- ♦ 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 guidelines (below) in Table 1 (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)

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

Cautions

- ♦ Use actual body weight or maximum body weight whichever is lower.
For maximum body weight table see <https://www.sapg.scot/media/4471/maximum-body-weight-table.pdf>
- ♦ In patients with low creatinine (< 60 micromol/L), use 60 micromol/L.
- ♦ Note: Use of estimated glomerular filtration rate (eGFR) is not recommended

LOADING DOSE

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.

Volumes used are for peripheral administration. More concentrated solutions (10mg/ml) must be given via a central line.

N.B. The loading dose is based on weight only so does not take account of renal function. When using the on-line calculator, on rare occasions a patient's clearance of vancomycin may be so high that the maintenance dose is higher than the 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.

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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).
- ♦ In order to facilitate the more convenient timing of administration and monitoring of vancomycin, the FIRST maintenance dose may be given up to 6 hours earlier (if 12 or 24 hourly dosing) or up to 12 hours earlier (if 48 hourly dosing). Please see table below for further details.

Table 2: Vancomycin MAINTENANCE dosage regimen

VANCOMYCIN PULSED INFUSION - INITIAL MAINTENANCE DOSAGE GUIDELINES				
CrCl (mL/min)	Dose amount	Volume of sodium chloride (0.9%)*	Dose interval	Time window for starting FIRST maintenance dose
< 20	500 mg over 1 hour	250 mL	48 hours	36-48 hours post loading dose
20 - 29	500 mg over 1 hour	250 mL	24 hours	18-24 hours post loading dose
30 - 39	750 mg over 1.5 hours	250 mL	24 hours	18-24 hours post loading dose
40 - 54	500 mg over 1 hour	250 mL	12 hours	6-12 hours post loading dose
55 - 74	750 mg over 1.5 hours	250 mL	12 hours	6-12 hours post loading dose
75 - 89	1000 mg over 2 hours	250 mL	12 hours	6-12 hours post loading dose
90 - 110	1250 mg over 2.5 hours	250 mL	12 hours	6-12 hours post loading dose
>110	1500 mg over 3 hours	500 mL	12 hours	6-12 hours post loading dose

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

Doses of up to 2000mg can be diluted in 500ml fluid for peripheral administration.
More concentrated solutions (10mg/ml) must be given via a central line.

- ♦ 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.
For example, 1500 mg 12 hourly (3000 mg per day) could be prescribed as 1000 mg 8 hourly and 750 mg 12 hourly (1500 mg per day) as 500 mg 8 hourly.

Note that patients who have unusual clinical characteristics, e.g. weight < 40 kg, weight >120 kg, age >90 years may require dose adjustments and require close monitoring. Contact pharmacy for advice.

Intravenous Vancomycin Use in Adults Intermittent (Pulsed) Infusion

STEP 2:

Monitor the vancomycin concentration and reassess the dosage regimen

Concentrations are meaningless unless the dose & 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 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 prescribing chart AND on the sample request form.
- ♦ If 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 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 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, 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

Vancomycin concentration	Suggested dose change
<10 mg/L	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
>20 mg/L	Withhold until <20 mg/L then seek advice

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

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General points

- ◆ Record the exact times of all measured concentrations on the vancomycin prescription chart.
- ◆ 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 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.