

Paediatric Medication Guideline

Intravenous Vancomycin

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Responsible Area	Pharmacy department Infection Management and Prevention Service			Review date	23/02/2025
Executive sponsor	Executive Director Medical Services				
Accountable Officer	Executive Director Clinical Services				

Purpose

To provide guidance around the clinical use of intravenous Vancomycin in paediatric patients under the care of/as recommended by Children's Health Queensland (CHQ).

Scope

This guideline is intended to assist all clinical staff to prescribe, administer and monitor intravenous Vancomycin appropriately. It is not intended to be a substitute for specific professional or clinical advice, or to replace consultation with senior staff, which should always be sought if clinically relevant.

This material is published by Queensland Health with the intention of providing a guideline for use in paediatric patients under the care of/as recommended by Children's Health Queensland (CHQ). Anyone wishing to use this guideline outside CHQ should refer to their local Medicines Committee before using.

Description and Indications for Use

Vancomycin, a glycopeptide antibiotic, is an essential antibiotic in the treatment of infections with certain Gram-positive microorganisms, particularly where there is suspected or proven antibiotic resistance.

All patients requiring more than 48 hours of Vancomycin, need Infectious Diseases (ID) input and [approval](#) to receive ongoing therapy. Pre-approved indications are specified on the [CHQ Antimicrobial stewardship website](#).

Clinicians should be aware that vancomycin is less effective than beta-lactam antibiotics for beta-lactam-susceptible staphylococci and therefore vancomycin is not recommended for therapy if a beta-lactam alternative exists.

Glycopeptides are also an alternative class of antibiotics for use in patients with a known severe immediate type hypersensitivity to beta-lactam antibiotics under the guidance of the ID team.

To ensure efficacy, minimize toxicity and limit the spread of resistance, it is essential that vancomycin treatment is prescribed and monitored carefully.



Prescribing Instructions

X	<h3>Contraindications</h3> <ul style="list-style-type: none"> Known hypersensitivity to vancomycin or any of the excipients or other glycopeptides. Redman syndrome is not a contra-indication – refer to Precautions.
!	<h3>Precautions</h3> <h4>Ototoxicity</h4> <ul style="list-style-type: none"> Although ototoxicity secondary to vancomycin is uncommon, vancomycin should be used with caution with concomitant ototoxic medications (e.g., aminoglycosides, frusemide, cisplatin). <h4>Nephrotoxicity</h4> <ul style="list-style-type: none"> Risk of nephrotoxicity is increased with concomitant use of other nephrotoxic medications and certain comorbidities. <h4>Renal risk factors:</h4> <ul style="list-style-type: none"> Dehydration or significant blood loss Concomitant nephrotoxic medicines (including aminoglycosides, amphotericin, diuretics, ACE inhibitors, NSAIDs, recent IV contrast media, tacrolimus, cyclosporin, nephrotoxic chemotherapy) Poor renal perfusion due to depressed cardiac function/heart failure/ critical illness/septic shock Receiving renal replacement therapy (CRRT, ECMO, Haemodialysis, peritoneal dialysis, plasmapheresis) Severe liver disease increasing risk for hepatorenal syndrome Paediatric studies have demonstrated that patients receiving intermittent vancomycin dosing with trough levels exceeding 15mg/L are at 2.7-fold increased risk for developing acute kidney injury, especially when Vancomycin is given in conjunction with beta-lactam antibiotics such as piperacillin/tazobactam. Renal function and hydration should be closely monitored. Pre-existing renal impairment and obesity are also risk factors for nephrotoxicity

Before starting intravenous Vancomycin

- Check baseline creatinine, urea and electrolytes (CHEM20, CHEM8)
- Assess [renal risk factors](#) and renal perfusion (urine output)
- Use Modified Schwartz formula to calculate Paediatric Creatinine Clearance (CrCl)**:

$$\text{CrCl (mL/min/1.73m}^2\text{)} = [36.5 \times \text{Height (cm)}] / \text{Creatinine (micromol/L)} = \text{_____ mL/min/1.73m}^2$$

**Not validated to be used in children under 1 year of age

Daily review whilst on Vancomycin IV therapy

Clinicians must answer the following questions DAILY for any patient receiving vancomycin IV:

- Is vancomycin the most appropriate IV antibiotic based on clinical condition and microbiology results?
 - If not, is an alternative antibiotic more appropriate? Seek ID advice.
- Is the current dose of vancomycin appropriate for indication, renal function and hydration status?
 - If not, perform therapeutic drug monitoring (TDM) and seek expert advice.

Prescribing initial intermittent Vancomycin IV dose

Dosing Guidance for initiating vancomycin as intermittent IV dosing at outset of therapy			
Patient population	Initial Dose and dose frequency (Dose based on actual body weight)	Timing of initial trough level	
Neonates	Refer to Australasian Neonatal Medicines formulary (ANMF) – Vancomycin (intermittent dosing) neonatal monograph for dosing information. Note: Neonate on ECMO - seek ID/ PICU expert advice on dosing and monitoring		
Infants and children with normal renal function (CrCl <u>more than or equal to</u> 60mL/min/1.73m ²)	15mg/kg/dose (Maximum 750 mg) IV 6 hourly Critically ill patients presenting with septic shock or patients with obesity: A single IV loading dose of 25 to 30 mg/kg (maximum dose of 1500 mg) could be considered in patients with septic shock or obesity or as directed by ID. If a loading dose is given, it should be counted as the first dose.	Trough level (30 minutes pre dose) pre 4 th dose. Take level and then give dose. Do not withhold dose. Patients with renal risk factors or obesity, take trough level pre 3 rd dose. Discuss with Treating team if dose should be withheld until level returns. Patients with septic shock in PICU or with confirmed MRSA bacteraemia, AUC monitoring is preferred. Seek ID/expert advice.	
Infants and children with renal insufficiency (CrCl less than 60mL/min/1.73m ²)	Creatinine clearance (CrCl) (Modified Schwartz)	Initial Dose: 15mg/kg/dose (Maximum 750mg)	Trough level (30 minutes pre dose) pre 2 nd dose WAIT for the result before giving the next dose
		Initial dose frequency	
	51 to 59 mL/min/1.73m ²	6 hourly	
	30 to 50 mL/min/1.73m ²	12 hourly	
	10 to 29 mL/min/1.73m ²	24 hourly	
< 10 mL/min/1.73m ²	Seek ID/ expert advice		
Infants and children on peritoneal (CAPD) or haemodialysis (HD)	Give a single dose of 15mg/kg (Maximum 500mg) IV (if HD, give post dialysis) and seek ID/expert advice.	Trough level at 24 hours* post dose. If high flux HD is used, seek nephrologist/expert advice	
Infants and children receiving CRRT or ECMO (PICU)	If CrCl \geq 60 mL/min/1.73m²: 15mg/kg/dose (Maximum 750 mg) IV 6 hourly. Seek ID/expert advice. If CrCl < 60mL/min/1.73m²: Refer to “Infants and children with renal insufficiency” and seek ID/expert advice.	Seek ID/expert advice. Trough level (30 minutes pre dose) pre 2 nd dose WAIT for the result before giving the next dose	
Peri-operative prophylaxis	Single peri-operative dose for specified procedures as per CHQ-GDL-01064 CHQ Paediatric surgical antibiotic prophylaxis guidelines	TDM only required if therapy is ongoing – ID consultation and approval required for ongoing use.	
Obesity: For obese children with body mass index (BMI) for age and sex of 95 th percentile or more, use actual (measured) bodyweight. A loading dose may be beneficial in this patient cohort. Monitor for signs of nephrotoxicity. * Assess renal risk factors (see Precautions on page 2)			

Prescribing initial Vancomycin Continuous IV infusion

- ID Consultant advice and approval required prior to commencement of Vancomycin continuous infusion.
- If commencing Vancomycin as continuous infusion at outset of therapy, give loading dose immediately followed by continuous infusion.
- If patient has been established on intermittent IV Vancomycin, seek ID/expert advice for conversion to continuous IV infusion (dose adjustment may be required).

Dosing Guidance for initiating vancomycin as <u>continuous infusion at outset of therapy</u> ^{15^A}			
Patient population	Loading dose		Starting dose for 24-hour continuous infusion
Neonates	Refer to Australasian Neonatal Medicines formulary (ANMF) – Vancomycin (continuous IV infusion) neonatal monograph for dosing information		
Infants and children with normal renal function (CrCl more than or equal to 60mL/min/1.73m ²)	15mg/kg IV as a single dose (Maximum 750mg)		60 mg/kg/day (Maximum 3000 mg/ 24 hours)
Infants and children with renal insufficiency (CrCl less than 60mL/min/1.73m ²)	Creatinine Clearance (Modified Schwartz)	Loading dose	Starting dose for 24-hour continuous infusion
	51 to 59 mL/min/1.73m ²	15 mg/kg (Max 750 mg)	60 mg/kg/day (Maximum 3000 mg/ 24 hours)
	30 to 50 mL/min/1.73m ²	15 mg/kg (Max 750 mg)	30 mg/kg/day (Maximum 1500 mg/ 24 hours)
	10 to 29 mL/min/1.73m ²	7.5 mg/kg (Max 375 mg)	15 mg/kg/day (Maximum 750 mg/ 24 hours)
< 10 mL/min/1.73m ²	Not recommended		

Administration Instructions

Reconstitution/Dilution

Refer to [Paediatric injectable guidelines – Vancomycin monograph](#).

Route and Method of Administration

Refer to [Paediatric injectable guidelines – Vancomycin monograph](#).

Clinical Considerations

Adverse Reactions

Redman syndrome

Rapid infusion may cause red man syndrome; symptoms include flushing or rash on the upper body and neck, muscle spasm of the chest and back.

If this occurs:

- Cease infusion and notify medical officer
- Assess for signs of anaphylaxis (i.e. urticaria, stridor, wheeze)
 - If these are present, manage as an anaphylactic reaction, including IM adrenaline.
 - In these cases, vancomycin must be avoided in the future. Consider referring to QPIAS Drug allergy service for assessment.
- If no signs of anaphylaxis are present,
 - check dosage and infusion rate
 - wait for symptoms to resolve
 - reduce infusion concentration, if possible
 - resume infusion at a slower rate
 - Future infusions should be administered over at least 3 to 4 hours
- [Report and document adverse reaction](#)

Extravasation risk

Intravenous vancomycin may cause venous irritation and tissue necrosis if the infusion infiltrates/extravasated. If the infusion “tissues”, the skin around the infusion site is red or the patient indicates any pain or discomfort, suspend the infusion and seek immediate medical review. Print [CHQ-PROC-60579 Extravasation and Infiltration](#) and follow the instructions for medical review and the subsequent recommendations for management. Seek specialised clinical review even if the injury looks minor.

Therapeutic Drug Monitoring

General principles

- Consider patient’s clinical condition and risk factors for toxicity (for example, concomitant nephrotoxic agents, IV contrast media, dehydration/fasting status, existing renal dysfunction).
- Dose recommendations are based on attainment of the targets.
- In patients with stable renal function
 - Vancomycin exhibits linear pharmacokinetics; an increase or decrease in dose should result in a proportionate increase or decrease in plasma concentrations.
 - Repeat levels once or twice a week in patients with stable renal function.
- In critically ill patients (for example: patients with septic shock, oncology patients, cardiac patients)
 - Renal clearance may be altered (either impaired or augmented renal clearance observed). Take care with dose adjustments in these patient groups.
 - Repeat levels every 48 to 72 hours or more frequently if rapidly changing renal function or critically ill patient.
- In patients with renal impairment

- The frequency of dosing should be extended and levels should be checked before the next dose is administered. Seek specialist advice.

Timing of levels for patient receiving Vancomycin as intermittent IV dosing

Patients with normal renal function

Trough level:

- Trough level should be taken at steady state wherever possible. Ideal sampling time is 30 minutes prior to dose.
- Take trough level (30 minutes prior to dose – see Table 1) and then give the next dose. Do not withhold dose, as this will delay the time to achieve therapeutic concentrations.

If continuing therapy, subsequent trough levels should be performed in children with normal renal function:

- 24 hours (or prior to the 4th dose) following a dose change.
- Every third day if continuing therapy at the same dose and the patient is stable.
- Once two plasma concentration measurements (taken 24 to 48 hours apart) are in therapeutic range, monitor vancomycin levels at least twice weekly in stable patients.

Patients with renal impairment or renal risk factors

Trough level:

- Trough level should be taken at steady state wherever possible. Ideal sampling time is 30 minutes prior to dose.
- Take trough level (30 minutes prior to dose – see Table 1, mark sample as urgent and send to pathology for analysis). Withhold the next dose until the level result returns and is reviewed by the Medical team/Pharmacist.

Sampling technique:

Vancomycin levels can be taken as a finger prick, heel prick or from a suitable Central venous access device (CVAD, for example PORT-a-cath, CVL or PICC line) using the correct technique.

Patient on intermittent Vancomycin IV with a CVAD in-situ

Flush CVAD with 5 to 10mL sodium chloride 0.9%, then withdraw an equal volume from the CVAD to discard, before taking a fresh sample from the CVAD for the Vancomycin level.

This technique will reduce the risk of sample contamination and reporting of falsely high results.

Therapeutic targets and dose adjustments for Vancomycin intermittent IV dosing

Adjusting doses in patients with normal renal function with UNCOMPLICATED INFECTIONS		
<ul style="list-style-type: none"> Haemodynamically stable patient on empirical therapy, no MRSA risk factors or coagulase negative staphylococcus bacteraemia Therapeutic target: Trough level 7 to 10 mg/L (accept 7 to 13mg/L) Ensure timing of samples and sampling method is appropriate, when interpreting results 		
Measured trough level (mg/L) (30 minutes pre-dose)	Dose adjustment	Next level
< 6 mg/L	Increase dose by 20 %	Repeat level pre 4th dose after dose change. Notify ID team if levels remain <10mg/L despite dose adjustment.
7 to 13 mg/L	No dose change	Repeat trough in 48-72 hours
14 to 20 mg/L	Reduce dose by 15-20% OR change dose frequency (e.g., from 6-hourly to 8-hourly or 8-hourly to 12-hourly).	Repeat level pre 3 rd dose after dose/ interval change and check renal function.
More than 20 mg/L	Withhold next dose	Repeat level in 6 to 8 hours and renal function. Continue to withhold dose until results return. If repeat level is more than 13mg/L, continue to withhold and repeat level in 6 hours. Seek ID/expert advice.

Severe renal impairment or patients on renal replacement therapy:

- Take trough level before 2nd dose (30 minutes pre-dose) and continue to withhold dose until trough level is less than or equal to 15 mg/L before re-dosing. Seek ID/expert advice.

Therapeutic targets and dose adjustments for Vancomycin intermittent IV dosing (continued)

Adjusting doses in patients with normal renal function with COMPLICATED INFECTIONS		
<ul style="list-style-type: none"> MRSA bacteraemia, meningitis, septic shock, bone/joint infection or infective endocarditis Therapeutic target: Trough level 15 to 20mg/L (accept 14 to 21mg/L) Ensure timing of samples and sampling method is appropriate, when interpreting results 		
Measured trough level (mg/L) (30 minutes pre-dose)	Dose adjustment	Next level
< 9 mg/L	Increase dose by 25-30 %	Repeat level pre 4th dose after dose change. Notify ID team if levels remain < 14mg/L despite dose adjustment.
10 to 13 mg/L	Increase dose by 15-20 %	Repeat level pre 4th dose after dose change. Notify ID team if levels remain < 14mg/L despite dose adjustment.
14 to 21 mg/L	No dose change	Repeat trough in 48-72 hours*
22 to 25 mg/L	Extend dosing interval (e.g., from 6-hourly to 8-hourly, or 8-hourly to 12-hourly).	Repeat level pre 3 rd dose after dosing interval change and check renal function*.

More than 25 mg/L	Withhold next dose	<p>Repeat level in 6 to 8 hours and check renal function*. Continue to withhold dose until results return.</p> <p>If repeat level is 15-20mg/L, then restart at 25% lower dose (or adjust dose interval – e.g. from 6-hourly to 8-hourly or 8-hourly to 12-hourly). Repeat trough level in 24 hours.</p> <p>If repeat level is more than 20mg/L, continue to withhold and repeat level in 6 hours. Seek ID/expert advice.</p>
<p>*Note: Paediatric studies have demonstrated that patients with vancomycin trough levels exceeding 15mg/L are at 2.7-fold increased risk for developing acute kidney injury, especially when Vancomycin is given in conjunction with beta-lactam antibiotics such as piperacillin/tazobactam.</p>		

Area Under the Curve monitoring^{2,3,11,13}

Indication: Confirmed MRSA bacteraemia or complicated infections under guidance of ID SMO

AUC target: AUC/MIC = 400 to 600 mg.hr/L (for MRSA with an MIC of 1mg/L)

Sampling time (steady state):

- Peak level = 2 hours post dose
- Trough level = 30 minutes pre-dose

Considerations:

- **Unless a health service has expertise with AUC monitoring, it is recommended that trough plasma concentrations are used to guide dosing.**
AUC monitoring should only be used upon ID consultant advice
- If a Bayesian predictive model is used for AUC-based dose optimisation, two samples (usually a peak and trough) should be used because, in children, this appears to improve accuracy and precision compared with single-sample estimates.
- Paediatric research is ongoing in this area. Please consult your ID specialist/AMS pharmacist/Specialist pharmacist for advice.

Therapeutic targets and dose adjustments for Vancomycin continuous IV infusion

Vancomycin continuous infusions demonstrate a linear relationship between the total daily dose (mg/day) and the corresponding steady state plasma concentration (mg/L).

Vancomycin continuous infusion target

- C_{ss} (Steady state concentration) = 17 to 25 mg/L (equates to AUC/MIC 400 to 600 mg.hr/L)

Timing of first level

- Take steady state level (C_{ss}) approximately 18 to 24 hours from commencement of continuous infusion.

Repeat levels

- Repeat C_{ss} level 24 hours after infusion rate/dose adjustment
- In patients with normal renal function who are clinically stable, repeat levels every 72 hours
- In patients with renal impairment, monitor levels every 24-48 hours as directed by ID specialist

Sampling technique

Patient on Vancomycin continuous IV infusion with CVAD in-situ

Pause continuous infusion for at least 10 minutes, then flush CVAD with 5 to 10mL sodium chloride 0.9%, then withdraw an equal volume from the CVAD to discard, before taking a fresh sample from the CVAD for the Vancomycin level.

This technique will significantly reduce the risk of sample contamination and reporting of falsely high results. If spurious levels reported, pause vancomycin continuous infusion for 10 minutes, then take a new blood sample as a finger prick or venepuncture from the opposite limb (not from CVAD).

Additional Information

Electronic prescribing in ieMR

Prescriber to use [Paediatric Vancomycin Power Plan](#) to prescribe Vancomycin and order first Vancomycin level by placing an electronic pathology order.

The prescriber or pharmacist should also place a '[Medication Level placeholder](#)' which will appear on the Medication Administration Record (MAR) - this acts as a task reminder to the nursing staff when a medication level is due to ensure optimal collection time.

In patients with normal renal function

- Take Vancomycin level and then proceed with next dose. Vancomycin level must be checked and dose adjustments made (if needed) before the following dose is given.

In patients with renal impairment or renal risk factors

- Take Vancomycin level and then withhold the next dose until the level returns and is reviewed by the Treating team and/or Pharmacist.

Documenting therapeutic drug monitoring results and plan

Prescriber or Pharmacist to document a Vancomycin Therapeutic drug monitoring (TDM) note in the patient's electronic medical record with details on interpretation of results and recommendation for dose adjustment/further monitoring.

Example of Vancomycin TDM note template below:

Vancomycin Therapeutic drug monitoring – note

Indication for treatment: _____

- Day of therapy = _____
- Intended duration of treatment (if known) = _____
- Current IV dose and frequency = _____

Current renal function: _____

Renal risk factors (see guideline and specify)

Vancomycin therapeutic target (see guideline and specify which target is used)

- Uncomplicated infection – trough 7 to 10 mg/L
- Complicated infection – trough level 15 to 20 mg/L
- AUC/MIC 400 to 600 mg.hr/L (under ID consultant guidance)

Vancomycin TDM results:

- Level taken (date/time)
- Sample taken from (specify - finger prick, heel prick, venepuncture, CVAD)
- Result = ___mg/L

Interpretation of results: _____

Recommendations: _____

Discussed with (specify) _____

Handover provided to (specify) _____

Reviewed by:

Signature

Supporting documents

Procedures, Guidelines and Protocols

- CHQ-PROC-01036 [Antimicrobial: Prescribing and Management](#)
- CHQ [Antimicrobial restrictions](#)
- CHQ-PROC-01001 [Medication – Prescribing](#)
- CHQ-PROC-01039 [Medication- Administration](#)
- CHQ [High Risk Medication List](#)
- CHQ-PROC-60579 – [Extravasation and Infiltration](#)

Consultation

Key stakeholders who reviewed this version:

- Pharmacist Advanced – Antimicrobial Stewardship
- Director – Infection Management and Prevention service (IMPS)
- Paediatric Nephrologist
- Paediatric Oncologist
- Paediatric Intensivist
- Pharmacist Lead – Oncology
- Pharmacist Lead – Medical
- Pharmacist Lead – Critical care
- Pharmacist Lead – Surgical
- CHQ Medicines Advisory Committee 16/02/2023

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Revision and approval history

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1.0	Pharmacist Advanced – Antimicrobial Stewardship	CHQ Medicines Advisory committee	Executive Director Clinical services
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Accreditation references	NSQHS Standards (1-8): 4 – Medication Safety, 3- Healthcare associated infections and Antimicrobial stewardship ISO 9001:2015 Quality Management Systems: (4-10)