Joint Trust Guideline for the Use of Intravenous Vancomycin in Paediatrics

Document Control:

For Use In:	Norfolk and Norwich University Hospitals (NNUH), James Paget University Hospitals (JPUH)		
	All clinical areas where vancomycin is prescribed for Children aged 1 month to 16 years – All medical, nursing, pharmacy, microbiology, and phlebotomy paediatric staff		
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Version	Date	Author	Reason/Change
3	January 2023	Consultant Paediatrician	Changes to dosing and frequency of administration Updated to new Trust Docs template

Previous Titles for this Document:

Previous Title/Amalgamated Titles	Date Revised
None	Not applicable

Note which Trust, where applicable.

Distribution Control

Printed copies of this document should be considered out of date. The most up to date version is available from the Trust Intranet.

Consultation

The following were consulted during the development of this document:
Dr. Priya Muthukumar, Chief of Service – Paediatrics NNUH
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Monitoring and Review of Procedural Document

The document owner is responsible for monitoring and reviewing the effectiveness of this Procedural Document. This review is continuous however as a minimum will be achieved at the point this procedural document requires a review e.g. changes in legislation, findings from incidents or document expiry.

Relationship of this document to other procedural documents

This document is a clinical guideline applicable to Norfolk and Norwich University Hospitals and James Paget University Hospitals; please refer to local Trust's procedural documents for further guidance.

Guidance Note

This guideline has been approved by the Trust's Clinical Guidelines Assessment Panel as an aid to the diagnosis and management of relevant patients and clinical circumstances. Not every patient or situation fits neatly into a standard guideline scenario and the guideline must be interpreted and applied in practice in the light of prevailing clinical circumstances, the diagnostic and treatment options available and the professional judgement, knowledge and expertise of relevant clinicians. It is advised that the rationale for any departure from relevant guidance should be documented in the patient's case notes.

The Trust's guidelines are made publicly available as part of the collective endeavour to continuously improve the quality of healthcare through sharing medical experience and knowledge. The Trust accepts no responsibility for any misunderstanding or misapplication of this document**.**

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1. Introduction

1.1. Rationale

Vancomycin is a narrow spectrum, glycopeptides antibiotic with potent anti-staphylococcal activity. Vancomycin is potentially ototoxic and nephrotoxic, and it must be prescribed and monitored carefully. This guideline offers advice on vancomycin dosing and monitoring in patients with normal renal function.

1.2. Objective/s

The aim of this guideline is to offer guidance on vancomycin dosing and monitoring for children aged 1 month to 16 years old.

1.3. Scope

This guideline covers the use of intravenous vancomycin prescribed for paediatric patients (1 month to 16 years old).

1.4. Glossary

The following terms and abbreviations have been used within this document:

Term	Definition
NNUH	Norfolk and Norwich University Hospitals
JPUH	James Paget University Hospitals
MRSA	Methicillin-resistant Staphylococcus aureus
BNFc	British National Formulary for Children
EIA	Equality Impact Assessment

2. Responsibilities

2.1. Paediatric Medical Staff

Paediatric medical staff are responsible for prescribing Vancomycin according to this guideline.

2.2. Paediatric Nursing Staff

Paediatric nursing staff are responsible for administering Vancomycin according to this guideline.

2.3. Paediatric Pharmacists

Paediatric pharmacists are responsible for auditing compliance and checking prescriptions and administration against this guideline.

3. Processes to be followed

3.1. Broad recommendations

Vancomycin should only be used if indicated, which will be informed by the patient's clinical condition, the Antibiotic Policy and any microbiological reports and sensitivity pattern of the organisms if available.

Patients with an impaired renal function must be treated with a reduced dose of vancomycin according to their renal function.

Patients must have their vancomycin levels and renal function monitored according to the guidelines below.

3.2. Background

Vancomycin is a glycopeptide antimicrobial. It is essential and invaluable in the management of infections due to MRSA and coagulase negative staphylococci, Staphylococcus aureus and other Gram-positive organisms in penicillin allergic patients. Resistance in staphylococci and enterococci has been reported. This has serious implications for patient care.

It is therefore imperative that vancomycin is used prudently by clinicians. This will ensure that patients receive maximum benefit from these agents and resistance and side effects minimised.

3.3. Indications for Use

Vancomycin should be prescribed where a glycopeptide antibiotic is specifically required or recommended. Vancomycin is potentially ototoxic and nephrotoxic. The risk of toxicity increases with high plasma concentration, concomitant use of nephrotoxic agents, reduced perfusion medications, patients with extended use of vancomycin > 14days, patients receiving chemotherapy protocols employing nephrotoxic agents or protocols that require an intact renal clearance of chemotherapies. Toxicity also increases in patients with a renal transplant or single kidney and patients with reduced renal perfusion.

This guideline offers advice on dosing and monitoring of vancomycin in children with normal renal function.

For further advice contact Microbiology.

3.4. Vancomycin Dosing (normal renal function)

In the BNFc, the intravenous dose for vancomycin depends on age, renal function and weight. A loading dose may be required in seriously ill patients under the direction of a Consultant Paediatrician.

Age	Dose (for pts with eGFR <90ml/min see page 4 for guidance)
1 month-11 years	**10-15mg/kg every 6 hours** (Adjusted according to plasma concentration monitoring) Doses higher than 60mg/kg/day cannot be generally recommended as the safety of the increasing dosing have not been fully assessed. *Duration should be tailored to type and severity of infection and the individual clinical response*.
12-17years	**15-20mg/kg every 8-12 hours (max. per dose 2g)** (Adjusted according to plasma concentration monitoring) *Duration should be tailored to type and severity of infection and the individual clinical response.*
Loading Dose Information This decision to give a loading dose should be in discussion with the on-call Paediatric Consultant	In seriously ill patients, a loading dose of 25-30mg/kg (usual max dose 2g) may be used to facilitate rapid attainment of the serum trough target serum vancomycin concentration. The maintenance dose should then be started at the correct dosing interval afterwards, e.g. 8 hours or 12 hours depending on the schedule chosen.

3.5. Vancomycin Monitoring

a. **First Level:** Take a pre-dose (trough) level before the **4th** dose. (Approximate time to reach steady state is 1-2 days). If renal function is stable, give the next dose before the trough results is available.

b. **Serum Creatinine:** Measure serum creatinine within 24 hours after initiating vancomycin to verify renal function and repeat twice weekly. If an increase in serum creatinine ≥ 45 micromoles/L from baseline is noted, serum vancomycin trough levels should be monitored more closely (i.e., no less than three times per week or as the dosing changes/permits. Dose reduction and/or increase in dosing interval should be considered).

c. **Check blood urea and provide fluids** to correct any pre-renal issues to ensure patient has adequate hydration within 24 hours of starting Vancomycin.

d. **Further levels**: If the trough is within the normal range (see below) and renal function remains stable, repeat trough levels twice weekly. If ≥ 30% unintended increase in vancomycin trough occurs (i.e., while on therapy without dose changes), then serum trough levels and serum creatinine should be monitored more closely, and dose reduction considered.

Serum Vancomycin Level (mg/L)	Dose Adjustment Advice
<5	Confirm all doses given as prescribed If no missed doses, increase dose by 50% Re-check the level before the **4th dose** after the change
7.5-10	Confirm all doses given as prescribed If dosing is 6 hourly increase dose by 30% and continue with same dosing interval If dosing is 8 hourly continue at same dose and change dosing interval to 6 hourly. If dosing is 12 hourly, continue at same dose and change dosing interval to 8 hourly Re-check the level before the **4th dose** after the change
10-20	**In therapeutic range.** For less sensitive strains of MRSA and for some cases of infective endocarditis (on microbiology advice) or deep seated infection the target range is 15-20mg/L For pts with stable renal function repeat level in 3 days
20-25	Confirm samples taken appropriately. Omit the dose until level is <20mg/L If dosing interval is 6 hourly change interval to 8 hourly If dosing is 8 hourly or less frequent, reduce next dose by 30% and continue with current dosing interval. Re-check the level before the **4th dose** after the change (or sooner if renal function deteriorates)
>25	Confirm samples taken appropriately If so, withold the next dose, take repeat level 12 -24 hours later and wait until level falls to <20mg/L Reduce next dose by 50% Discuss with a Pharmacist regarding dosing interval and rechecking levels. .

3.6. Things to consider when interpreting Vancomycin Levels for unexpected results

- Was the blood sample taken at the correct time, and is it a true trough specimen?
- Was the blood sample taken from the intravenous line used to infuse vancomycin?
- Was vancomycin used as a line lock?
- Has the patients' renal function or hydration status deteriorated or improved?

3.7. Patients under the care of the Renal Team

Patients with eGFR <90ml/min/1.73m2 are at greater risk of toxicity. This includes patients on dialysis. The below gives dosing recommendations for patients with renal impairment. Please refer to the renal team or liaise with Nottingham renal team for advice.

Calculating eGFR

$$\text{eGFR (mL/min/1.73m}^2\text{)} = \frac{35 \times \text{height in cm}}{\text{Serum creatinine (micromol/L)}}$$

Initial Dosing Recommendations (taken from Nottingham policy, dated May 2020)

Age	eGFR 51-90mL/min/1.73m^2	eGFR 16-50mL/min/1.73m^2	eGFR 15mL/min/1.73m^2 or less, OR on dialysis
35 weeks corrected gestational age-to 6 months	**10mg/kg 8 hourly**	**15mg/kg as a single dose.** Check level 24 hours later and re-dose when level <20mg/L	**7.5mg/kg as a single dose.** Check level 24 hours later and re dose when level <20mg/L. Give after dialysis in those on haemodialysis.
6 months to 1 year	**15mg/kg 8 hourly** Pre dose level before 3rd dose. 3rd dose can be given without knowing the result. Do not give 4th dose until result is known	**15mg/kg as a single dose**. Check level 24 hours later and re-dose when level <20mg/L	**7.5mg/kg as a single dose.** Check level 24 hours later and re dose when level <20mg/L. Give after dialysis in those on haemodialysis
1 year to 6 years	**17.5mg/kg 8 hourly**	**15mg/kg as a single dose.** Check level 24 hours later and re-dose when level <20mg/L	**7.5mg/kg as a single dose.** Check level 24 hours later and re dose when level <20mg/L. Give after dialysis in those on haemodialysis
Over 6 years	**15mg/kg (max 750mg) 8 hourly**	**15mg/kg (max 750mg) as a single dose.** Check level 24 hours later and then re-dose when level <20mg/L	**7.5mg/kg (max 500mg) as a single dose.** Check level 24 hours later and re dose when level <20mg/L. Give after dialysis in those on haemodialysis

3.8. Administration Details for Vancomcyin

Reconstitute each 500mg of vancomycin vial with 9.6mL of water for injection (0.4mL displacement) and is further diluted with 5% glucose or 0.9% sodium chloride infusion so that the final concentration is no greater that 500mg per 100mL (**5mg/mL)** to minimize infusion-related side effect such as thrombophlebitis. 10mg/mL concentration can be if infused via central venous line over at least 60 minutes.

The required dose is administered over at least 60 minutes (rate not to exceed over **10mg/min** for doses over **500mg**). Infuse over 120 minutes with antihistamine cover for patients with previous reactions (red man syndrome)

Nurses should state on the drug chart the exact time of administration to facilitate the accurate interpretation of levels

3.9. Further Advice

During working hours contact Microbiology on extension 4587 or 4589 or the paediatric ward pharmacist.

Out of hours contact the on-call microbiologist (bleep via switchboard) or on call pharmacist (bleep via switchboard).

4. References

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5. Audit of the process

Compliance with the process will be monitored through the following:

Key elements	Process for Monitoring	By Whom (Individual / group /committee)	Responsible Governance Committee /dept	Frequency of monitoring
All children over the age of one month when vancomycin is the drug of choice should be given vancomycin in a dose appropriate recommended in BNFc (the dosing schedule described in this guideline).	Audit	Medical/Pharmacy staff	Paediatric Governance Committee	Yearly
The form accompanying the sample (pre-dose only) must state the time the sample was taken and the time of the start of the previous infusion.	Audit	Medical/Pharmacy staff	Paediatric Governance Committee	Yearly
Medical notes should reflect review of the dosing regimen depending on vancomycin levels.	Audit	Medical/Pharmacy staff	Paediatric Governance Committee	Yearly
Vancomycin levels should be taken at the appropriate time depending on the dosing regimen.	Audit	Medical/Pharmacy staff	Paediatric Governance Committee	Yearly

The audit results are to be discussed at relevant governance meetings (Paediatric Clinical Governance) to review the results and recommendations for further action. Then sent to Antimicrobial Subgroup Committee who will ensure that the actions and recommendations are suitable and sufficient

6. Equality Impact Assessment (EIA)

Type of function or policy	New/Existing (remove which does not apply)

Division	3	**Department**	Paediatrics
Name of person completing form	Caroline Hallam	**Date**	8.6.23

Equality Area	Potential Negative Impact	Impact Positive Impact	Which groups are affected	Full Impact Assessment Required YES/NO
Race	None	None	None	No
Pregnancy & Maternity	Contraindication of certain medications in pregnancy and breastfeeding	None	N/A	No
Disability	None	None	None	No
Religion and beliefs	None	None	None	No
Sex	None	None	None	No
Gender reassignment	None	None	None	No
Sexual Orientation	None	None	None	No
Age	Dosage based on age	Dosage based on age	Dosage based on age	No
Marriage & Civil Partnership	None	None	None	No
EDS2 – How does this change impact the Equality and Diversity Strategic plan (contact HR or see EDS2 plan)?				

- **A full assessment will only be required if: The impact is potentially discriminatory under the general equality duty**
- **Any groups of patients/staff/visitors or communities could be potentially disadvantaged by the policy or function/service**
- **The policy or function/service is assessed to be of high significance**

IF IN DOUBT A FULL IMPACT ASSESSMENT FORM IS REQUIRED

The review of the existing policy re-affirms the rights of all groups and clarifies the individual, managerial and organisational responsibilities in line with statutory and best practice guidance.