MONOGRAPH

Vancomycin (intravenous) Monograph – Paediatric

Scope (Staff):	Medical, Pharmacy, Nursing
Scope (Area):	All Clinical Areas

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this DISCLAIMER

⚠ HIGH RISK MEDICINE ⚠

Vancomycin is a **high risk medicine** which may cause or aggravate renal dysfunction.
ALL patients prescribed IV vancomycin must have daily review to ensure ongoing use is appropriate.

1. *Has the appropriate vancomycin dose and frequency been prescribed?*
2. *Does the patient commencing or continuing vancomycin have abnormal creatinine and if so, have appropriate dose modifications been made?*
3. *Is the child adequately hydrated and are all concurrent nephro-toxins discontinued where possible?*
4. *Has a vancomycin trough level **with** serum creatinine been checked and appropriate dose modifications enacted?*
5. *Can the vancomycin be ceased? (request relevant microbiological samples for microscopy, culture and susceptibility testing early and check if the patient is previously colonised with MRSA [Microalert B/C], if unknown consider MRSA swabs of the nose, groin and axillar where there is clinical concern or higher risk patients.)*

QUICKLINKS

DRUG CLASS

Glycopeptide antibiotic.[1-3]

Vancomycin is a High Risk Medicine.

INDICATIONS AND RESTRICTIONS

Vancomycin is indicated in the empiric and directed treatment of Methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-resistant coagulase-negative staphylococcal species and in patients with a high risk allergy to beta-lactams.[2, 4]

IV: Monitored (orange) antibiotic

- Vancomycin is indicated for use as per the indications stipulated in Formulary One. For any other use, phone approval must be obtained from ChAMP before prescribing as per the Antimicrobial Stewardship Policy.

CONTRAINDICATIONS

- Hypersensitivity to vancomycin, teicoplanin or any component of the formulation. Allergic cross reactivity has occurred between vancomycin and teicoplanin.[2, 5-9]
- Vancomycin must **not** be given via intramuscular or subcutaneous injection as it may cause ulceration and necrosis.[10]

Note: Vancomycin Flushing syndrome is a histamine mediated reaction and is not considered an allergy, however the infusion time should be extended – see administration section for further information.[7, 9, 10]

PRECAUTIONS

- Risk factors for nephrotoxicity and impaired vancomycin clearance include patients with pre-existing renal impairment, sepsis, vomiting, fasting, dehydration or haemodynamic instability. Concurrent use of nephrotoxic drugs (e.g. piperacillin/tazobactam, furosemide, aciclovir, aminoglycosides [e.g. gentamicin], amphotericin, ciclosporin and IV contrast), increase the risk of vancomycin associated nephrotoxicity.[2, 5, 6, 9]
- Vancomycin should be used cautiously with other ototoxic medications (e.g. aminoglycosides, furosemide, cisplatin). Ototoxicity may be more common in patients with renal impairment. Pre-existing hearing loss may increase risk of ototoxicity from vancomycin.[2, 5, 7, 9]
- General anaesthetics may increase the risk of vancomycin infusion related adverse events including hypotension. When used for surgical prophylaxis, vancomycin should be commenced at least 15 minutes prior to knife to skin.[2, 4, 7]
- Beware of extravasation as this may cause tissue necrosis.[5, 6, 10]
- Previous thrombocytopenia during vancomycin or teicoplanin treatment may recur as it may be immune-mediated.[2]

FORMULATIONS

Listed below are products available at PCH, other formulations may be available, check with pharmacy if required:

- 500 mg Vancomycin powder for injection vial
- 1 gram Vancomycin powder for injection vial ® – Pharmacy Compounding Service (PCS) use only

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS

Neonates: **Refer to Neonatal Medication Protocols**

Dosing in Overweight and Obese Children: For empirical use of vancomycin, dose obese patients using their **ideal** body weight and make dose adjustments according to vancomycin therapeutic drug monitoring (TDM).[5, 11] For children with confirmed MRSA invasive infection, discuss with Infectious Diseases for further advice.

IV – Children ≥ 4 weeks:

Intermittent dosing:

- **Initial dose:** 15 mg/kg/dose (to a maximum of 750 mg) 6 hourly.[1, 2, 9]
- Note – loading doses are not routinely used in paediatric patients.

Continuous infusion: refer to **Appendix A**.

Surgical prophylaxis:

- Single dose 15 mg/kg/dose (to a maximum of 750 mg) via slow infusion (see administration section for further information).[5, 9]
- Vancomycin infusion should be started within 120 minutes before surgical incision (ideally at least 15 minutes before incision) to ensure adequate blood and tissue concentrations at the time of incision and to allow potential infusion-related toxicity to be recognised before induction of anaesthesia. The infusion can be completed after surgical incision.[4, 5, 9]

Oral: Please refer to the oral vancomycin monograph.

Renal impairment:

- eGFR calculator
- In patients with impaired renal function treatment should be initiated at 15 mg/kg/dose (maximum dose of 750 mg) with *suggested initial* intervals as detailed below.
- **In those with renal impairment, therapeutic drug monitoring is required prior to the 2nd dose being administered.**[5, 6, 8]

Dose adjustment table:

eGFR	Dose
≥50 mL/minute	Use standard initial dose
≥30 to < 50 mL/minute/1.73 m^2	15 mg/kg/dose (maximum dose of 750 mg) 12 hourly
≥10 to <30 mL/minute/1.73 m^2	15 mg/kg/dose (maximum dose of 750 mg) 24 hourly
< 10 mL/minute/1.73 m^2	15 mg/kg as a single dose (maximum dose of 750 mg) with subsequent doses based on therapeutic drug monitoring.[12]

Hepatic impairment:

- No dosage adjustment is required in hepatic impairment.[6]

Dosage adjustment for patients on Extracorporeal Membrane Oxygenation (ECMO):

- The optimal dose and frequency of patients on ECMO has not been established. Frequent monitoring of levels is recommended.[6]

Dosage adjustment for patients receiving multiple infusions:

- Occasionally, due to competing needs for other infusions, the dose and frequency of vancomycin administration may need to be altered. In a child with normal renal function, twice daily dosing is a valid dosing schedule and may be considered in this situation (i.e. 30 mg/kg/dose up to a maximum of 1.5 g TWICE daily). Discuss with Infectious Diseases (ID) for further advice and recommendations for therapeutic drug monitoring.[2]

RECONSTITUTION & ADMINISTRATION

IV reconstitution:

- Reconstitute each vial with the volume of water for injection in the table below. Further dilution with compatible fluid to a final concentration of 5 mg/mL is required prior to administration.[5, 7, 10]

Vial strength	Volume of water for injections required	Resulting concentration
500 mg	10 mL	50 mg/mL
1000 mg	20 mL	50 mg/mL

- Use solution prepared by Pharmacy Compounding Service (PCS) when possible.

Intermittent IV infusion:

- Dilute with compatible fluid to a final concentration of 5 mg/mL or less. Doses < 600 mg should be infused over one hour. Doses ≥ 600 mg should be infused at a rate of 10 mg/minute.[2, 7, 10]
- A final concentration of 10 mg/mL may be used if the patient is fluid restricted AND has a central venous access device in-situ.[10] However this higher concentration increases the risk of thrombophlebitis and infusion related reactions.[5, 10]
- If Vancomycin Flushing Syndrome occurs, future infusion times should be extended (minimum duration 2 hours). Antihistamine use prior may prevent the syndrome.[10]

Continuous infusion:

- **Refer to Appendix A**

COMPATIBILITY *(LIST IS NOT EXHAUSTIVE)*

Compatible fluids:

- Glucose 5% and 10%
- Sodium chloride 0.9%
- Hartmann's[7, 10]

Compatible at Y-site:

Compatibilities of IV drugs must be checked when two or more drugs are given concurrently.

MONITORING

- All patients require regular therapeutic drug monitoring (TDM) of vancomycin as outlined below, with concurrent serum creatinine. A complete blood count should be collected least weekly in patients with normal renal function and more frequently in patients with any degree of renal impairment. Reversible neutropenia has been reported in patients receiving vancomycin for longer than one week. Leucocytes should be monitored in patients undergoing prolonged therapy with vancomycin.[2, 3, 7, 8]
- A capillary blood sample is preferred for drug levels wherever possible (i.e. finger prick or heel prick for infants <6 months). If unable to obtain via this method a venous sample can be taken.
- Serum creatinine must be checked at the same time or within the 12 hours prior to every vancomycin level. Patients fluid status should also be monitored.[5]

Collection tube:

- Serum, no gel (RED)
- Minimum volume required: 400 microlitres.[13]
- Sample should be taken in the 60 minutes before administration of the next dose.[6]

Vancomycin trough targets:

- **Intermittent infusion:** Aim for a trough level between 5-15 mg/L.[6, 14]

Patients with confirmed invasive methicillin resistant *Staphylococcus aureus* infections: Discuss antimicrobial therapy with Infectious Diseases and consider a continuous infusion in patients with severe MRSA infection, as well as area under the curve (AUC) monitoring of vancomycin.[15, 16]

Continuous infusions: refer to **Appendix A**.

Therapeutic drug monitoring (TDM):

*(i) Normal renal function and **not** at risk of developing renal impairment*:

- Immediately prior to the 4th dose with serum creatinine taken at the same time or within the previous 12 hours.[6]
- If no adjustments and normal creatinine, then a repeat vancomycin trough and serum creatinine should be performed every 2-3 days whilst on therapy.

(ii) Renal impairment or patients with risk factors for developing renal impairment (e.g. sepsis, dehydration, vomiting, fasting, pre-existing renal impairment, on concomitant nephrotoxic agents such as piperacillin/ tazobactam, gentamicin or aciclovir) [4]:

- Early trough vancomycin level collected and checked prior to the 2nd dose with a serum creatinine level taken at the same time **(do not increase dose based on this level).**
- If stable and ongoing risk factors, repeat trough levels with serum creatinine daily.
- If elevated, refer to monitoring section and discuss with Infectious Diseases for further advice.

(iii) Patients on dialysis for acute kidney injury or continuous renal replacement therapy (CRRT):

- Vancomycin level at 24 hours and wait for result before administering the next dose. Please discuss with Infectious Diseases.

Initial dose adjustment based on TDM (for intermittent dosing)[4]:

- Prior to adjusting any doses check;
    - The trough level was taken appropriately in the 60 minutes prior to dose being due for administration**.**
    - The most recent serum creatinine is within the normal range AND is not trending upwards.
    - Daily review of the need for ongoing vancomycin is required with consideration to cease where appropriate.

Trough plasma concentration	**Based on initial dose of 15mg/kg/dose 6 hourly**
<5 mg/L	Increase dose to 20 mg/kg/dose 6 hourly (maximum 80 mg/kg/day or 3 grams per day).[a]
≥ 5 to <15mg/L	Maintain current dose.

≥ 15mg/L to <20mg/L	Maintain current dose if no renal impairment and repeat vancomycin trough and creatinine the next day. If concomitant renal impairment withhold dose and repeat trough level approximately 8 hours after the last level (preferably within hours) and recommence vancomycin if ongoing therapy is required when trough <15 mg/L at a 10-20% dose reduction.[b]
≥ 20mg/L to <25mg/L[b]	Withhold dose until level is <15 mg/L (unless on a continuous vancomycin infusion). Repeat trough level approximately 8 hours after the last level (preferably within hours) and recommence vancomycin if ongoing therapy is required when trough is <15 mg/L at a 20-30% dose reduction.
≥ 25mg/L[b]	Withhold dose until level is <15 mg/L and investigate cause of high level and consider if ongoing vancomycin therapy is required. Repeat trough level approximately 8 to 16 hours after the last level (preferable within hours). When trough is <15 mg/L recommence if ongoing therapy is required at a 30-50% dose reduction. *A clinical incident report (via Datix CIMS) must be submitted by the treating team for* (i) all vancomycin levels >40 mg/L OR (ii) vancomycin levels >25 mg/L with evidence of associated renal impairment

[a] For patients who are already receiving the maximum dose of 80 mg/kg/day or 3 grams per day, contact Infectious Diseases/ChAMP for advice.

[b] If further advice is required, contact Infectious diseases/ChAMP.

Monitoring for continuous infusions:

- Refer to **Appendix A**

Audiology monitoring:

- Audiology monitoring should be considered in patients requiring ≥ 2 weeks therapy, who receive high or toxic levels (>25 mg/L), who receive concurrent ototoxic medications or in those with underlying hearing loss.[8]

ADVERSE EFFECTS

Infusion related reactions (Vancomycin Flushing Syndrome) is a histamine mediated infusion related reaction that occurs when vancomycin is administered too quickly. Symptoms include fever, chills, erythema, rash (particularly of head, neck and upper chest) and may be followed by hypotension, angioedema and itch. If further doses are required, the infusion rate should be slowed. Pre-treatment with an antihistamine may also assist.[2, 3, 10]

Common: Nausea, vomiting, abdominal pain, diarrhoea, local pain, thrombophlebitis, infusion related reactions (include; hypotension, palpitations, tachycardia, fever, dizziness, pruritus, rash, flushing), hypokalaemia, hypersensitivity reactions (include rash, chills, itch, rigors, eosinophilia, angioedema).[2]

Infrequent: nephrotoxicity[2]

Rare: thrombocytopenia, neutropenia (more common after >1 week of therapy), leucopenia, agranulocytosis, interstitial nephritis, *Clostridioides difficile*-associated disease, anaphylaxis, hypersensitivity reactions (including; chills, urticaria, severe cutaneous adverse reactions (SCARs), eosinophilia, angioedema, vasculitis, fever and rigors), ototoxicity, drug reaction with eosinophilia and systemic symptoms (DRESS).[2]

STORAGE

Vials for reconstitution: Store below 25˚C and protect from light.[10]

Solutions prepared by PCS: Store between 2˚- 8˚C.[10]

INTERACTIONS

This medication may interact with other medications; consult PCH approved references (e.g. Clinical Pharmacology), a clinical pharmacist or PCH Medicines Information Service on extension 63546 for more information.

Please note: The information contained in this guideline is to assist with the preparation and administration of **vancomycin (intravenous)**. Any variations to the doses recommended should be clarified with the prescriber prior to administration

Related CAHS internal policies, procedures and guidelines

Antimicrobial Stewardship Policy

ChAMP Empiric Guidelines and Monographs

KEMH Neonatal Medication Protocols

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Appendix A: Vancomycin continuous infusions

DOSAGE & DOSAGE ADJUSTMENTS

Continuous infusions:

- Continuous infusions are prescribed to achieve target trough levels in invasive MRSA infections or to assist patients to transfer to the Hospital in the Home (HiTH) service. Discuss with Infectious Diseases for further advice.
- The daily dose of vancomycin continuous infusion should be the total amount of vancomycin administered over the previous 24 hours. In cases of low serum levels, a dose increase is not recommended when initially converting to a continuous infusion but may be discussed with Infectious Diseases following appropriate TDM.[1]
- Dosing must be rounded to the nearest 100 mg to facilitate preparation of the infusion.

Refer to main table for all dose adjustments

RECONSTITUTION & ADMINISTRATION

Continuous infusion: Dilute to a final concentration of 5 mg/mL and infuse over 24 hours.[10]

Dose of vancomycin	Fluid bag required	Volume of excess fluid to remove	Volume of compatible fluid to add	Volume of vancomycin 50 mg/mL to add	Final volume required to achieve final concentration of 5mg/mL
300mg	50mL	3mL		6 mL	60 mL
400mg	100mL	36mL		8 mL	80 mL
500mg	100mL	18mL		10mL	100 mL
600mg	100mL			12 mL	120 mL
700mg	100mL		18mL	14 mL	140 mL
800mg	100mL		36mL	16 mL	160 mL
900mg	100mL		54mL	18 mL	180 mL
1000mg	250mL	85 mL		20 mL	200 mL
1100mg	250mL	67 mL		22 mL	220 mL
1200mg	250mL	49 mL		24 mL	240 mL
1300mg	250mL	31 mL		26 mL	260 mL
1400mg	250mL	13 mL		28 mL	280 mL
1500mg	250mL		5mL	30 mL	300 mL
1600mg	250mL		23mL	32 mL	320 mL
1700mg	500mL	239 mL		34 mL	340 mL
1800mg	500mL	221 mL		36 mL	360 mL
1900mg	500mL	203 mL		38 mL	380 mL
2000mg	500mL	185 mL		40 mL	400 mL
2100mg	500mL	167 mL		42 mL	420 mL
2200mg	500mL	149 mL		44 mL	440 mL
2300mg	500mL	131 mL		46 mL	460 mL
2400mg	500mL	113 mL		48 mL	480 mL
2500mg	500mL	95 mL		50 mL	500 mL

2600mg	500mL	77 mL	[redacted]	52 mL	520 mL
2700mg	500mL	59 mL		54 mL	540 mL
2800mg	500mL	41 mL		56 mL	560 mL
2900mg	500mL	23 mL		58 mL	580 mL
3000mg	500mL	5 mL		60 mL	600 mL

Note:

- 50 mL bag (Baxter) has a 7 mL overage (total initial volume is 57 mL)
- 100 mL bag (Baxter) has an 8 mL overage (total initial volume is 108 mL)
- 250 mL bag (Baxter) has a 15 mL overage (total initial volume is 265 mL)
- 500 mL bag (Baxter) has a 45 mL overage (total initial volume is 545 mL)

COMPATIBILITY *(LIST IS NOT EXHAUSTIVE)*

Compatible fluids:

- Glucose 5% and 10%
- Sodium chloride 0.9%
- Hartmann's[10, 12]

Compatible at Y-site:

Compatibilities of IV drugs must be checked when two or more drugs are given concurrently.

MONITORING

Monitoring for continuous infusions:

- Serum vancomycin level should be measured in conjunction with serum creatinine at 24 and 48 hours following commencement of the infusion, with target levels between 17-25 mg/L.[14] Dose adjustments should be discussed with Infectious Diseases/ChAMP. Once stable repeat levels in conjunction with serum creatinine every three days throughout treatment.

Refer to main table for further monitoring requirements