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 ⚠

QUICKLINKS

SUMMARY

Vancomycin is a **high risk medicine** which may cause or aggravate renal dysfunction. The ChAMP team will review and recommend cessation of vancomycin within 48 hours, unless required for ongoing targeted therapy and/or acceptable indications.

DAILY REVIEW

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

1. *Has the appropriate vancomycin dose and frequency been prescribed?*
2. *Does a 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?*

MONITORING:

Patient's baseline renal function must be determined. Ongoing monitoring of both vancomycin trough levels and renal function should occur at the following intervals:

Impaired renal function OR patients with risk factors for renal impairment:

- Includes pre-existing renal impairment, dehydration or sepsis .(1)
- These patients must have an early trough level collected and checked prior to the 2nd dose with a

serum creatinine level taken at the same time. If elevated, discuss with Infectious Diseases for ongoing dosing and monitoring recommendations.
- More frequent monitoring of vancomycin levels should be considered in patients on vancomycin in combination with other nephrotoxic drugs (e.g. combination therapy with vancomycin and piperacillin/ tazobactam.)

Normal renal function:

- Trough vancomycin level prior to the 4th dose with serum creatinine taken at the same time.
- If stable, repeat levels (with serum creatinine) every 3 days.

TROUGH LEVELS

- **Aim for a trough level between 5-15mg/L**
- **Patients with confirmed or suspected invasive methicillin resistant *Staphylococcus aureus* infections:** Discuss antimicrobial therapy with Infectious Diseases. Alternative therapy may be considered.

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 >25mg/L with evidence of associated renal impairment

DRUG CLASS

Glycopeptide antibiotic.[2]

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.[1, 2]

IV: Monitored (orange) antibiotic

- If the use is consistent with a standard approved indication, this must be communicated to ChAMP by documenting that indication on all prescriptions (inpatient and outpatient).
- The ChAMP team will review if ongoing therapy is required and/or if the order does not meet ChAMP Standard Indications
- If use is not for a standard approved indication, phone approval must be obtained from ChAMP before prescribing.

CONTRAINDICATIONS

- Hypersensitivity to vancomycin or any component of the formulation.[3]
- Vancomycin must **not** be given via intramuscular or subcutaneous injection as it may cause ulceration and necrosis.[4]

Note: Vancomycin Flushing syndrome (previously known as Red Man 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.[3, 4]

PRECAUTIONS

- Risk factors for nephrotoxicity and impaired vancomycin clearance include patients with pre-existing renal impairment, sepsis, 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 nephrotoxicity and vancomycin toxicity.

- 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, 3]
- Vancomycin should be used cautiously in patients with a history of a serious reaction to teicoplanin, cross reactivity has occurred between teicoplanin and vancomycin.[2, 3]
- General anaesthetics may increase the risk of vancomycin infusion related adverse events including hypotension.[2, 5].
- Beware of extravasation as this may cause tissue necrosis.[4]

FORMULATIONS

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

- 500mg Vancomycin powder for injection vial
- 1gram 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: Dose obese and overweight patients on actual body weight. Shorter dosing intervals may be required to maintain serum trough levels.[2]

Children ≥ 4 weeks:

Intermittent dosing:

- **Initial dose:** 15mg/kg/dose (to a maximum of 750mg) 6 hourly.[6]

Continuous infusion: refer to **Appendix A**

Surgical prophylaxis:

- Single dose 15mg/kg/dose (to a maximum of 750mg) via slow infusion (see administration section for further information).
- 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.[1]

Oral: Please refer to oral vancomycin monograph

Inhalation: Please refer to inhaled vancomycin monograph

Renal impairment:

- eGFR calculator (Google Chrome®)

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

Dose adjustment table:

eGFR	Dose
≥50mL/minute	Use standard initial dose
≥30 to < 50mL/minute/1.73m^2	15mg/kg/dose (maximum dose of 750mg) 12 hourly
≥10 to <30 mL/minute/1.73m^2	15mg/kg/dose (maximum dose of 750mg) 24 hourly
< 10mL/minute/1.73m^2	15mg/kg as a single dose (maximum dose of 750mg) with subsequent doses based on therapeutic drug monitoring.[7]

Hepatic impairment:

No dosage adjustment is required in hepatic impairment.[8]

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

Initial dosage for patients on ECMO should be 20mg/kg/dose every 24 hours due to an increased circulating volume and transiently altered renal function.[7] Contact Infectious Diseases/ChAMP for further advice.

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. 30mg/kg/dose up to a maximum of 1.5g TWICE daily). Discuss with Infectious Diseases (ID) for further advice and therapeutic drug monitoring.[2]

RECONSTITUTION & ADMINISTRATION

IV reconstitution:

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

- Dilute with compatible fluid to a final concentration of 5mg/mL or less.[4]
- Use solution prepared by Pharmacy Compounding Service (PCS) when possible.

Intermittent IV infusion:

- Dilute with compatible fluid to a final concentration of 5mg/mL or less. Doses < 600mg should be infused over one hour. Doses ≥600mg should be infused at a rate of 10mg/minute.[2, 4]
- A final concentration of 10mg/mL may be used if the patient is fluid restricted AND has a central venous access device in-situ.[4] However this higher concentration increases the risk of thrombophlebitis and infusion related reactions such as Vancomycin Flushing Syndrome (previously known as Red Man Syndrome - see 'Adverse effects' below).[4, 7, 8]
- If Vancomycin Flushing Syndrome (previously known as Red Man Syndrome) occurs, future infusion times should be extended (minimum duration 2 hours). Antihistamine use prior may prevent the syndrome.[2, 4]

Continuous infusion:

- **Refer to Appendix A**

COMPATIBILITY *(LIST IS NOT EXHAUSTIVE)*

Compatible fluids:

- Glucose 5% and 10%
- Sodium chloride 0.9%
- Hartmann's[4, 7]

Compatible at Y-site:

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

MONITORING

- 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.[8]

Collection tube:

- Lithium Heparin- PST (GREEN)

- Minimum volume required: 400microlitres.[9]

Vancomycin trough targets:

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

Patients with confirmed or suspected invasive methicillin resistant *Staphylococcus aureus* infections: Discuss antimicrobial therapy with Infectious Diseases.

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.
- If no adjustments and normal creatinine then a repeat vancomycin trough and serum creatinine should be performed every 2-3 days whilst on therapy [1]

(ii) Renal impairment (or patients with risk factors for developing renal impairment)

- Includes patients with pre-existing renal impairment, dehydration or sepsis
- **To exclude toxicity** - early vancomycin trough and serum creatinine taken and checked before administration of 2nd dose (**do not increase dose based on this level**).
- Consider daily vancomycin trough and creatinine monitoring in patients with existing renal impairment, please discuss with ID/ChAMP.
- More frequent monitoring of vancomycin levels should also be considered in patients on vancomycin in combination with other nephrotoxic drugs (e.g. combination therapy with vancomycin and piperacillin/ tazobactam.)

(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 ID/ChAMP.

Initial dose adjustment based on TDM (for intermittent dosing)[1]:

Trough plasma concentration	**Based on initial dose of 15mg/kg/dose 6 hourly**
<5 mg/L	Increase dose to 20mg/kg/dose 6 hourly (maximum 80mg/kg/day or 3 grams per day)*
≥ 5 to <15mg/L	Maintain current dose
≥ 15mg/L to <20mg/L	Dose reduction may be required. *Contact Infectious Diseases/ChAMP for further advice (including the ID on call service after hours).*
≥ 20mg/L to <25mg/L	Withhold dose until level is <20mg/L (unless on a continuous vancomycin infusion). *Contact Infectious Diseases/ChAMP for further advice (including the ID on call service after hours).*
≥ 25mg/L	Withhold dose until level is <20mg/L and investigate cause of high level. *Contact Infectious Diseases/ChAMP for further advice (including the ID on call service after hours).* *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 >25mg/L with evidence of associated renal impairment

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

Monitoring for continuous infusions:

- Refer to **Appendix A**

Additional monitoring for all patients:

- Audiology monitoring should be considered in patients requiring ≥ 2 weeks therapy, who receive high or toxic levels (>25mg/L), who receive concurrent ototoxic medications or in those with underlying hearing loss.[10]
- 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, 5, 10, 11]

ADVERSE EFFECTS

Vancomycin Flushing Syndrome (previously known as Red Man 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]

Common: Nausea, vomiting, abdominal pain, diarrhoea, local pain, thrombophlebitis, infusion related reactions (include; hypotension, palpitations, tachycardia, fever, dizziness, pruritus, rash, flushing), hypokalaemia.[2, 3, 10, 11]

Infrequent: nephrotoxicity[2, 3, 11]

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, 3, 10, 11]

STORAGE

Vials for reconstitution: Store below 25˚C and protect from light.[3, 4]

Solutions prepared by PCS: Store between 2˚- 8˚C.[4]

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 occasionally prescribed, particularly to achieve target trough level or to assist patients to transfer to the Hospital in the Home (HiTH) service. Discuss with Infectious Diseases for further advice.
- *Initial dose:* The recommended starting dose for vancomycin infusions is 60mg/kg/day (to a maximum of 3 grams over 24 hours). Higher doses may be considered in consultation with Infectious Diseases.
- Dosing must be rounded to the nearest 100mg to facilitate preparation of the infusion.

Refer to main table for all dose adjustments

RECONSTITUTION & ADMINISTRATION

Continuous infusion: Dilute to a final concentration of 5mg/mL and infuse over 24 hours.[4]

Dose of vancomycin	Fluid bag required	Volume of excess fluid to remove	Volume of compatible fluid to add	Volume of vancomycin 50mg/mL to add	Final volume required to achieve final concentration of 5mg/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		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:

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

COMPATIBILITY *(LIST IS NOT EXHAUSTIVE)*

Compatible fluids:

- Glucose 5% and 10%
- Sodium chloride 0.9%
- Hartmann's[4, 7]

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 20-25mg/L.[6] 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