Vancomycin Intravenous Monograph - Paediatric

**Scope (Staff):** Clinical Staff – Medical, Nursing, Pharmacy

**Scope (Area):** Perth Children’s Hospital (PCH)

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**Summary Page**

Vancomycin is a **high risk medication** 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 at risk of developing renal impairment:**
  - Includes pre-existing renal impairment, dehydration, sepsis and concurrent use of nephrotoxic drugs e.g. combination therapy with vancomycin + piperacillin/tazobactam
  - 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 or within the 12 hours prior. If elevated, discuss with Infectious Diseases for ongoing dosing and monitoring recommendations

- **Normal renal function:**
  - Trough vancomycin level prior to the 4th dose with serum creatinine taken at the same time or within the 12 hours prior.
  - If stable, repeat levels (with serum creatinine) every 3 days

**TROUGHS LEVELS**

1) **Confirmed/suspected invasive methicillin resistant Staphylococcus aureus infections:** 15-20mg/L
2) **All other infections:** 5-15mg/L

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**
### DESCRIPTION
Vancomycin is a glycopeptide antibiotic which inhibits bacterial cell wall synthesis by preventing the formation of peptidoglycan polymers. Vancomycin also alters the bacterial cell membrane permeability and RNA synthesis.\(^1\), \(^2\)

### INDICATIONS AND RESTRICTIONS
Vancomycin is active against Gram-positive bacteria, including methicillin-resistant Staphylococcus aureus (MRSA), methicillin-resistant coagulase-negative staphylococcal species and penicillin-resistant Streptococcal or Enterococcal species.\(^3\), \(^4\)

**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.

### CONTRA-INDICATIONS
Vancomycin is contraindicated in patients with a history of serious allergy to vancomycin.\(^2\)

**Note:** Red Man’s syndrome is not considered an allergy, however the infusion time should be extended – see administration section for further information.\(^1\)

Vancomycin must **not** be given via intramuscular or subcutaneous injection due to the risk of ulceration and necrosis.\(^5\)

### 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 (frusemide), aciclovir, aminoglycosides (e.g. gentamicin), amphotericin, ciclosporin (cyclosporine) and IV contrast) also increase the risk of nephrotoxicity and vancomycin toxicity.

Vancomycin should be used cautiously with other ototoxic medications (e.g. aminoglycosides, furosemide [frusemide], cisplatin). Ototoxicity may be more common in patients with renal impairment.\(^2\) Pre-existing hearing loss may increase risk of ototoxicity from vancomycin.\(^2\)

Vancomycin should be used cautiously in patients with a history of a serious reaction to teicoplanin, cross reactivity has occurred between teicoplanin and vancomycin.\(^2\)

General anaesthetics may increase the risk of vancomycin infusion related adverse events including hypotension. Ensure vancomycin infusion is complete before induction.\(^2\), \(^6\)

Beware of extravasation as this may cause tissue necrosis.\(^5\)

### FORMULATIONS
**Available at PCH:**
- 500mg Vancomycin powder for injection vial (Alphapharm brand\(^8\))
- 1g Vancomycin powder for injection vial (Alphapharm and DBL brand\(^8\))
  – Pharmacy Compounding Service (PCS) use only

**Other formulations available:**
- 500mg and 1g Vancomycin powder for injection vial; multiple generic brands.
### DOSAGE

The doses listed below fall within the standard range. Higher doses may be prescribed for certain situations in consultation with Infectious Diseases or Clinical Microbiology.

**Doses should be based on the patients actual body weight in obese or overweight patients.**\(^2\) Please see: [Guidelines For Drug Dosing in Overweight and Obese Children](#)

**Neonates (<1 month of age):**
- Please refer to [neonatal clinical care drug protocols](#)

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

**Continuous infusions:**
- Continuous infusions are occasionally prescribed, particularly 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.

**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 approximately 2 hours PRIOR to ‘knife to skin’ to achieve therapeutic levels.\(^7\)

**Oral:** Please refer to [oral vancomycin monograph](#)

**Inhalation:** Please refer to [inhaled vancomycin monograph](#)

### DOSAGE ADJUSTMENT

**Dose adjustment in overweight or obese patients:**
Dose obese patients based on actual body weight – shorter dosing intervals may be required to maintain serum trough levels.\(^2\)

Refer to [Guidelines For Drug Dosing in Overweight and Obese Children](#)

**Dosage adjustment is required in cases of impaired renal function:**
To calculate the estimated glomerular filtration rate (eGFR) use the formula available via the following link.\(^4\) This formula should only be used for children older than one year.

\[
eGFR (\text{mL/min/1.73m}^2) = \frac{36.5 \times \text{height (cm)}}{\text{Serum creatinine (micromol/L)}}
\]

This formula is based on a steady state creatinine clearance and is not applicable to patients with a dynamic serum creatinine.

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. **Therapeutic drug monitoring is required prior to the 2\textsuperscript{nd} dose being administered.**
## Dose adjustment table:

<table>
<thead>
<tr>
<th>eGFR</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>70-89mL/minute/1.73m²</td>
<td>15mg/kg/dose (maximum dose of 750mg) 8 hourly</td>
</tr>
<tr>
<td>30-69mL/minute/1.73m²</td>
<td>15mg/kg/dose (maximum dose of 750mg) 12 hourly</td>
</tr>
<tr>
<td>15-29mL/minute/1.73m²</td>
<td>15mg/kg/dose (maximum dose of 750mg) 24 hourly</td>
</tr>
<tr>
<td>&lt; 15mL/minute/1.73m²</td>
<td>15mg/kg as a single dose (maximum dose of 750mg) with subsequent doses based on therapeutic drug monitoring. (8)</td>
</tr>
</tbody>
</table>

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

Initial dosage for patients on ECMO should be 20mg/kg/dose every 24 hours. (8, 9) 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.

## RECONSTITUTION

### IV:

<table>
<thead>
<tr>
<th>Vial strength</th>
<th>Volume of water for injections required</th>
<th>Resulting concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>500mg</td>
<td>10mL</td>
<td>50mg/mL</td>
</tr>
<tr>
<td>1000mg</td>
<td>20mL</td>
<td>50mg/mL</td>
</tr>
</tbody>
</table>

Dilute with compatible fluid to a final concentration of 5mg/mL (or 10mg/mL if fluid restricted). Refer to administration section for further information. (5)

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

## ADMINISTRATION

### Intermittent IV infusion:

- Dilute to a final concentration of 5mg/mL or less and infuse over 60 minutes or 10mg/minute whichever is longer. Maximum rate of infusion is 10mg/minute. (5)

- If the patient is fluid restricted, a maximum concentration of 10mg/mL may be given via a central line. However this higher concentration increases the risk of thrombophlebitis and infusion related reactions such as Red Man Syndrome (see ‘Adverse effects’ below). (5)

- If Red Man Syndrome occurs, future infusions should be administered over at least 2 hours. Antihistamine use prior may prevent the syndrome. (5)
<table>
<thead>
<tr>
<th>Continuous infusion:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dilute to a final concentration of 5mg/mL or less and infuse over 24 hours. (5)</td>
</tr>
</tbody>
</table>

**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 within the 12 hours prior to every vancomycin level. Patients fluid status should also be monitored. (5, 6)

**Collection tube:**

- Paediatric - Lithium Heparin (Green top) 1 mL (PST gel) or Serum (Red top) 1 mL (No Gel)
- Neonatal - Lithium Heparin (Green top) 600 microlitres (PST gel)
- Minimum volume required: 400 microlitres (10)

**Vancomycin trough targets:**

- **Confirmed invasive MRSA infections:** 15-20mg/L (3)
  - These infections may warrant higher vancomycin trough targets (15-20mg/L). Early consultation with Infectious Diseases is recommended.
- **Other infections:** 5-15mg/L (3)
  - The standard range is safe and effective for most infections.

For continuous infusions seek advice from ID/ChAMP

**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 within 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 (4)

(ii) *Renal impairment (or at risk of developing renal impairment***)

- Includes patients with pre-existing renal impairment, dehydration, sepsis and concurrent use of nephrotoxic drugs e.g. combination therapy with vancomycin + piperacillin/tazobactam
- Early vancomycin trough and serum creatinine taken and checked before administration of 2nd dose (to exclude toxicity – do not increase dose based on this level.)
- Consider daily vancomycin trough and creatinine monitoring, please discuss with ID/ChAMP.

(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**
<table>
<thead>
<tr>
<th>Trough plasma concentration</th>
<th>Based on initial dose of 15mg/kg/dose 6 hourly</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5 mg/L</td>
<td><strong>All infections:</strong> Increase dose to 20mg/kg/dose 6 hourly (maximum 80mg/kg/day or 3 grams per day) .</td>
</tr>
<tr>
<td>≥ 5 to &lt;15mg/L</td>
<td><strong>Empirical use and non-MRSA infections:</strong> Maintain current dose <strong>Confirmed/suspected invasive MRSA infections</strong>: Increase dose to 20mg/kg/dose 6 hourly (maximum 3 grams per day) and contact Infectious Diseases/ChAMP for further advice (including the ID on call service after hours).</td>
</tr>
<tr>
<td>≥ 15mg/L to &lt;20mg/L</td>
<td><strong>Empirical use and non-MRSA infections:</strong> Recommend dose reduction. Contact Infectious Diseases/ChAMP for further advice (including the ID on call service after hours). <strong>Confirmed/suspected invasive MRSA infections</strong>: Maintain current dose</td>
</tr>
<tr>
<td>≥ 20mg/L to &lt;25mg/L</td>
<td><strong>Empirical use and non-MRSA infections:</strong> Withhold dose until level is &lt;20mg/L (unless on a continuous vancomycin infusion). Contact Infectious Diseases/ChAMP for further advice (including the ID on call service after hours). <strong>Confirmed/suspected invasive MRSA infections</strong>: Contact Infectious Diseases/ChAMP for advice (including the ID on call service after hours).</td>
</tr>
<tr>
<td>≥ 25mg/L</td>
<td><strong>All infections:</strong> Withhold dose until level is &lt;20mg/L and investigate cause of high level. Contact Infectious Diseases/ChAMP for further advice (including the ID on call service after hours).</td>
</tr>
</tbody>
</table>

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

** Suspected MRSA infection includes patients with gram positive cocci seen on gram stain from culture or those in the first 24-48 hour period, awaiting culture results, where there is a clinical indication for vancomycin as per the ChAMP guidelines.

**Monitoring for continuous infusions**: Serum vancomycin level should be measured with serum creatinine at 24 and 48 hours following commencement of the infusion, with target levels between 20-25mg/L. Dose adjustments should be discussed with Infectious Diseases/ChAMP. Once stable repeat levels with serum creatinine every three days throughout treatment.

**Additional monitoring for all patients**: Audiology should be considered in...
### Vancomycin monograph - paediatric

| ADVERSE EFFECTS | **Red man syndrome**: Red man syndrome is an 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. It is not an allergy and is related to the rate of the infusion. 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, nephrotoxicity, hypotension, palpitations, tachycardia, fever, dizziness, pruritus, rash, flushing, reversible neutropenia, inflammation or irritation of injection site, hypokalaemia.  
**Rare**: Interstitial nephritis, serious skin reactions, *Clostridium difficile* associated disease, anaphylaxis, hypersensitivity reactions (including; chills, urticaria, Stevens-Johnson syndrome, toxic epidermal necrosis, eosinophilia, angioedema, vasculitis, fever and rigors), ototoxicity, drug reaction with eosinophilia and systemic symptoms (DRESS), chemical peritonitis (with intra-peritoneal use). (1, 2, 11) |
| Compatible Fluids | • Glucose 5% and 10%  
• Sodium chloride 0.9%  
• Hartmann’s (5) |
| Storage | **Vials for reconstitution**: Store below 25˚C and protect from light. (5)  
**Solutions prepared by PCS**: Store between 2˚-8˚C (5) |
| Interactions | **Vancomycin has drug interactions; please consult PCH approved references (such as Clinical Pharmacology), your ward pharmacist or Pharmacy on extension 63546 for more information**  
• Vancomycin can cause nephrotoxicity and ototoxicity. Caution should be taken with the concurrent use of nephrotoxic and ototoxic agents. (2, 6)  
• General anaesthetics can increase the risk of vancomycin infusion related adverse events including hypotension. Ensure the vancomycin infusion is completed before induction. (2, 6)  
• Vancomycin may prolong the effects of suxamethonium, the dose of suxamethonium may require reduction. (2, 6)  
• The use of warfarin and vancomycin may increase the International Normalised Ratio (INR) and increase the risk of bleeding. (2, 6) |
| Manufacturer Safety Data Sheet (SDS) | To access the Manufacturer SDS for this product, use the following link to ChemAlert. |

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

File Path: \W\Safety & Quality\CAHS\CLOVERS MEDICAL Pharmacy\Procedures Protocols and Guidelines\ChAMP\Word\Monographs\PCH Templated (ED Guidelines)

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Reviewer / Team: Children's Antimicrobial Management Program Pharmacist

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