# VANCOMYCIN - SCH

## PRACTICE GUIDELINE ©

## DOCUMENT SUMMARY/KEY POINTS

- Vancomycin is used in situations of suspected or proven antibiotic resistance or allergy, and its appropriate use should be practiced
- This guideline outlines the indications, dosing, and monitoring of vancomycin

## CHANGE SUMMARY

- The doses and frequency for neonates have changed.
- The time of measuring the trough level has changed from prior to the fourth or fifth dose to “prior to the fifth dose”.
- The maximum dose of vancomycin has changed from 1 g per dose to 750 mg per dose.
- Therapeutic drug monitoring: revised recommendations.
- Target trough levels: Aim for a target trough level between 10-20 mg/L. Use the higher end of the range (15-20 mg/L) for severe or complicated infections.
- November 2015: minor review to correct a formatting issue in Section 4.

## READ ACKNOWLEDGEMENT

The following staff are to read and acknowledge they understand the contents of this document:

- All staff at SCH who are involved in the provision of antimicrobial agents to SCH patients.
- Clinical Department Heads and Nursing Unit Managers at SCH.

This document reflects what is currently regarded as safe practice. However, as in any clinical situation, there may be factors which cannot be covered by a single set of guidelines. This document does not replace the need for the application of clinical judgement to each individual presentation.

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| **Approved by:** | SCHN Policy Procedure and Guideline Committee | |
| **Date Effective:** | 1st November 2015 | **Review Period:** 3 year |
| **Team Leader:** | Staff Specialist | **Area/Dept:** SCH Infectious Diseases |

# TABLE OF CONTENTS

# 1 Background

Vancomycin, a glycopeptide antibiotic, is an essential antibiotic in the treatment of infections with some gram-positive microorganisms, particularly where there is suspected or proven antibiotic resistance. Glycopeptides are also an alternative class of antibiotics for use in patients allergic to beta-lactam antibiotics. Coagulase negative staphylococci, enterococci and more recently, *Staphylococcus aureus* have all been reported to exhibit varying degrees of resistance to vancomycin. In the interest of ensuring efficacy and limiting the spread of resistance, it is essential that appropriate and effective vancomycin treatment is used.[1]

# 2 Indications

***Vancomycin is appropriate or acceptable in the following situations:***[2-4]

- Treatment of serious infections due to beta-lactam-resistant gram-positive microorganisms.

  *Clinicians should be aware that vancomycin may be less bactericidal than beta-lactam agents for beta-lactam-susceptible staphylococci and therefore vancomycin is not recommended for therapy if an alternative exists*.

- Treatment of infections due to gram-positive microorganisms in patients with serious hypersensitivity (IgE-mediated or non IgE-mediated delayed type) to beta-lactam antimicrobials and other antimicrobial agents are not available.
  - *Immediate hypersensitivity is characterised by the development of urticaria, angioedema, bronchospasm or anaphylaxis (with objectively demonstrated hypotension, hypoxia or elevated mast-cell tryptase concentration) within 1 to 2 hours of exposure to a drug.*
  - *Delayed reaction: characterised by macular, papular or morbilliform rash, occurring several days after starting treatment. Examples include serum sickness, DRESS syndrome and Steven-Johnson syndrome.*
- For the rest of the indications for vancomycin use, see:
  - SCH Empiric Antibiotic Guideline.
  - SCH Guidance MS

# 3 Dose [4-7]

## 3.1 Neonates

| Postmenstrual age (NB1) | Postnatal age | Starting dose (use actual body weight) | Dosing frequency | Timing of trough level |
|---|---|---|---|---|
| < 30 weeks | 0-14 days | 15 mg/kg | 18-hourly | Before the second dose |
| | ≥ 14 days | | 12-hourly | Before the third dose |
| 30-36 weeks | 0-14 days | | 12-hourly | Before the third dose |
| | ≥14 days | | 8-hourly | Before the fourth dose |
| 37-44 weeks | 0-7 days | | 12-hourly | Before the third dose |
| | ≥7 days | | 8-hourly | Before the fourth dose |
| ≥ 45 weeks | | | 6-hourly | Before the fifth dose |

(NB1): postmenstrual age is the time elapsed between the first day of the last menstrual period and birth (gestational age) plus the time elapsed after birth (postnatal age).

## 3.2 Infants and Children

**IV: 15mg/kg/dose 6 hourly to a maximum of 750 mg per dose**

**NB:** A loading dose of 30 mg/kg can be considered in patients with severe sepsis. If a loading dose is given, it should be counted as the first dose

## 3.3 Infants and children with existing renal impairment or risk factors for toxicity

See: Patient with Renal Impairment or Risk Factors for Toxicity

# 4 Administration

Infuse over 2 hours in a concentration of no more than 5mg/mL.

In fluid restricted patients a concentration of 10mg/mL can be used. In patients receiving multiple IV medications, the infusion may be given over a shorter period but the rate of infusion must not be higher than 10 mg/minute. Patients with previous 'red man syndrome' may require longer infusion times (see Hypersensitivity reactions).

# 5 Vancomycin Toxicity

## 5.1 Nephrotoxicity

- Although nephrotoxicity with modern formulations of vancomycin is uncommon, concomitant use of vancomycin with nephrotoxic medications (e.g. aminoglycosides, amphotericin, cyclosporine, frusemide) increases this risk.
- Existing renal impairment is also a risk factor for nephrotoxicity.

## 5.2 Ototoxicity

- Although ototoxicity secondary to vancomycin is uncommon, vancomycin should be used with caution with concomitant ototoxic medications (e.g. aminoglycosides, frusemide, cisplatin).

## 5.3 Hypersensitivity reactions

- The most common hypersensitivity reaction is an infusion-related anaphylaxis-like reaction, known as 'red man syndrome'. This is characterised by flushing, erythema and pruritis, particularly of the upper body, head and neck. It is common and is related to the speed of infusion. The mechanism is direct mast cell activation by vancomycin. It is NOT a true, IgE-mediated allergy. However, anaphylaxis to vancomycin can present with similar signs.
- Suggested management of 'red man syndrome':
  - Stop the infusion.
  - 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.
  - If no signs of anaphylaxis are present, administer an antihistamine (e.g. cetirizine).
    - Once symptoms have subsided, the infusion can be re-started at one-half the original rate.
    - Future infusions of vancomycin should be administered over **four hours**. Consider pre-medicating with an antihistamine before infusions.

# 6 Monitoring Vancomycin

## 6.1 Background

- There is little evidence suggesting vancomycin nephrotoxicity occurs in children without risk factors, or that this toxicity is associated with high peaks.[8-13] Therefore, peak vancomycin levels should not be routinely measured.
- Trough levels should be measured to ensure effective antimicrobial levels are reached.
- A higher serum concentration (indicated by the trough level) may be required for effective antimicrobial activity in bone, joint or central nervous system infections.

## 6.2 Recommendations

- All children prescribed vancomycin should have their renal function checked either prior to commencing therapy or at the time of their first serum level.
- The first serum level should be performed **prior to the fifth dose** of vancomycin (i.e. when a "steady-state" is reached) in all children with normal renal function. A vancomycin trough level should be taken within 30 minutes before the next dose. See section 3.1 above for the timing of the trough level for neonates.
- In patients with normal renal function, **GIVE** the dose after taking the trough level. **DO NOT withhold** the next dose while awaiting the result as this usually results in the patient being under-dosed.
- A trough level should be performed in children with normal renal function **every third day** if continuing therapy is required and **prior to the fifth dose** following a dose change.
- To be able to interpret levels and adjust doses, the time the level is taken and the time the previous vancomycin dose was administered must be recorded.
- Target trough levels: Aim for a target trough level between **10-20mg/L**. Use the higher end of the range **(15-20 mg/L) for severe or complicated infections**.

## 6.3 Adjusting doses in children with normal renal function

- Trough level **above** the target range.

  If the trough vancomycin level is greater than the target range, the **total daily dose** should be **decreased by 20%, while the dosing interval remained at 6-hourly**. If the trough is **> 30mg/L**, check the patients renal function and discuss with the Infectious Diseases team before giving further doses.

- Trough level **below** the target range.

  If the vancomycin level is less than the target range, the **total daily dose** should be **increased by 20%, while the dosing interval remained at 6-hourly**. If the child has sepsis or CNS infection and the trough is still **< 10mg/L** despite dose adjustment, discuss with the Infectious Diseases team.

### 6.4 Adjusting doses in children with existing renal impairment or risk factors for toxicity.

See: Patient with Renal Impairment or Risk Factors for Toxicity

## 7 Patient with Renal Impairment or Risk Factors for Toxicity

Dosing and dose adjustment in patients with risk factors for toxicity, such as concurrent nephrotoxic drugs should be discussed with the Admitting Medical Officer.

### 7.1 Dose

- The dosing and interval of vancomycin depend on the estimated glomerular filtration rate.
- To estimate the dosing interval, the following table may be useful.[14]

Vancomycin excretion is influenced by glomerular filtration rate (GFR).

GFR can be estimated by the Schwartz formula:

$$\textbf{Estimated GFR} = \frac{\text{Height (cm)} \times 36.5}{\text{Serum creatinine (micromol/L)}}$$

| GFR (ml/min/1.73m$^2$) | Dose | Frequency |
|---|---|---|
| > 90 | 15 mg/kg | 6 hourly |
| 50 - 90 | 10 mg/kg | 12 to 24 hourly* |
| < 50 | 10 mg/kg | seek advice |

*A trough level should be performed prior to the **second dose** in children with renal impairment (GFR < 90 ml/min/1.73m$^2$) **WAIT** for the result before giving the next dose.

### 7.2 Vancomycin Monitoring and Dose Adjustment

- In children with existing renal impairment or risk factors for toxicity, renal function and drug monitoring are essential to guide therapy.
- If vancomycin level is below or above the target level, please seek advice from the Department of Nephrology or Infectious Diseases

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