

## Vancomycin Dosing in Adults

### Background

Vancomycin is a glycopeptide antibiotic that was first isolated in the early 1950s from *Streptomyces orientalis*, a bacterium discovered in a soil sample from a jungle path in Borneo. The following is an update on the therapeutics of intravenous vancomycin in adults.

### Indications

Intravenous vancomycin is used for the treatment of suspected or proven systemic Gram-positive infections that are generally resistant to other antibiotics (e.g. methicillin-resistant *staphylococcus aureus* (MRSA), coagulase-negative *staphylococci* ("coag -ve staph"), amoxicillin-resistant *enterococci*).

### Mechanism of Action

Vancomycin inhibits cell wall synthesis in bacteria by inhibiting peptidoglycan synthesis. The cell wall has a very important protective effect in Gram-positive bacteria, and if destroyed, the bacterium dies by osmotic lysis.

### Time-dependent killing

Vancomycin must reach a certain concentration (i.e. minimum inhibitory concentration, MIC) at the site of infection for it to be effective. The MIC for organisms such as MRSA, "coag -ve staph" and amoxicillin-resistant enterococci is typically around 1mg/L. The trough concentration of vancomycin in blood is kept above 5mg/L to ensure the concentrations are above the MIC at the site of infection. For 'deep' tissue infections (e.g. endocarditis, osteomyelitis), "peak" concentration monitoring and higher "trough" concentrations may be required to ensure concentrations at infection site are adequate – discuss these patients with Microbiology or Infectious Diseases (ID).

### Dosing

- **Loading dose:** 15mg/kg (based on lean body weight), irrespective of renal function.
- **Maintenance dose:** 30mg/kg/day (based on lean body weight) in patients with normal renal function. Vancomycin is almost entirely renally cleared, and therefore, the dose needs to be adjusted in renal impairment. Elimination of vancomycin is directly proportional to renal function.

The following table is a general guideline for dosing vancomycin. Use in patients with severe renal impairment should be discussed with the Ward Pharmacist or Clinical Pharmacology.

CrCl (mL/min)	Maintenance Dose	Interval (approx)	Total daily dose (mg/kg lean body weight)
> 90	500mg	6 hours	30mg/kg/day
	or 1g	12 hours	
71 - 90	750mg	12 hours	22.5mg/kg/day
51 - 70	500mg	12 hours	15mg/kg/day
25 - 50	750mg	24 hours	10mg/kg/day
10 - 24	500mg	24 hours	7.5mg/kg/day
< 10	Contact Ward Pharmacist or Clinical Pharmacology		

### Monitoring

After the second or third dose of vancomycin, a "trough" concentration should be measured around 30 minutes before the next dose and should be between 5-15mg/L. If the "trough" concentration is >15mg/L (unless higher concentrations have been requested by Microbiology/ID), or renal function deteriorates, a dose reduction and/or increase in dosing interval may be required. In stable patients, blood concentrations should be checked every 3 days.

### Administration

Vancomycin is given as an IV infusion over at least 1 hour, preferably at a rate no greater than 10mg/minute. (Rapid administration can cause "Red Man Syndrome" -see below). It also needs to be diluted (maximum concentration of 5mg/ml) to avoid pain and thrombophlebitis. For example, dilute a 1g dose in 250ml of diluent and give over 2 hours.

### Adverse effects

**"Red Man Syndrome":** Infusion of vancomycin >10mg/minute may cause "Red Man Syndrome". This is an infusion-related phenomenon and is characterised by flushing, erythema, and pruritis usually involving the upper body, neck, and face. Hypotension, dyspnoea, cardiac toxicity, and muscle spasms and pains in the back and chest may also occur. The cause is histamine release due to vancomycin directly activating mast cells. The response does not involve IgE and is not an allergic reaction. Therefore, the infusion may be resumed at a slower rate once symptoms have subsided.

**Nephrotoxicity** is thought to result from accumulation of vancomycin in renal cells and is usually reversible. The incidence is <5%, but increases to >40% in those receiving concomitant nephrotoxic medications (e.g. frusemide, aminoglycosides, amphotericin, ciclosporin). Nephrotoxicity is associated with concentrations >20mg/L.

**Ototoxicity** is manifested by vestibular damage and/or cochlear damage, leading to sensory hearing loss and tinnitus. Incidence is considered to be <5%. Reversible ototoxicity is generally associated with vancomycin concentrations >40mg/L, and irreversible ototoxicity with concentrations >80mg/L.

### Resistance

Resistance to vancomycin is an emerging problem. The number of vancomycin-resistant enterococci (VRE) cases reported in NZ from 1996-2006 were up to 6/year. In 2007, this increased to 69 cases and was attributed to a single outbreak. VRE microorganisms tend to be multi-drug resistant.

### Oral vancomycin

Vancomycin has poor oral availability and therefore passes through the gut. This is useful in *Clostridium difficile*-related diarrhoea and pseudomembranous colitis. Use is second-line, after failure of metronidazole. Vancomycin capsules are not available in NZ; instead the injection is given (diluted) orally.

### For further information:

For further information refer to your ward pharmacist or the Drug Information Service (ext 80900). Dosing and monitoring guidelines are in the 'Pink Book'.