Vancomycin – intermittent regimen

Newborn use only

2020

Alert	The Antimicrobial Stewardship Team recommends this drug is listed as: Restricted. Continuous infusion regimen optimises achievement of steady state target concentration with fewer dose adjustments and a lower total daily dose in comparison to intermittent regimen.
Indication	Infections due to susceptible strains of the following organisms: Staphylococci (including MRSA), Streptococci, Enterococci, Diptheroids, Listeria monocytogenes, Actinomyces, Bacillus spp.
Action	Bactericidal agent which interferes with cell wall synthesis, inhibits RNA synthesis and alters plasma membrane function.
Drug type	Glycopeptide antibiotic.
Trade name	DBL Vancomycin Hydrochloride, Vancocin CP, Vancomycin Alphapharm, Vancomycin AN powder for infusion.
Presentation	Vancomycin hydrochloride 500 mg vial Vancomycin hydrochloride 1000 mg vial
Dose	**Standard dose: 15 mg/kg/dose. Dosing interval as per table below**[24] **Severe sepsis:** Consider giving a loading dose of 20 mg/kg/dose in suspected severe sepsis e.g., MRSA, bone infection, meningitis, endocarditis. However, data in neonates are limited.
Dose - Special scenarios	**Renal Impairment:** • For infants with renal impairment, consider using an antibiotic without nephrotoxicity in consultation with an infectious diseases specialist. • If vancomycin is used, perform a trough level before the 2nd dose. • Adjust the dosage interval[5, 21] to achieve a trough level 10–20 mg/L (higher trough level 15–20 mg/L in severe sepsis). Repeat trough level before the next dose after each dosage adjustment or before every 3rd dose for infants within the target range. **Hepatic impairment:** Not applicable. **Therapeutic hypothermia:** Measure trough concentration prior to 2nd dose.[27] **ECMO:** Current evidence is insufficient to recommend a specific dose adjustment.
Maximum dose	Not applicable
Total cumulative dose	Not applicable
Route	IV
Preparation	**<u>500mg VIAL</u>** Add 10 mL of water for injection to the 500 mg powder for reconstitution to make a 50 mg/mL solution **Further Dilute:** Draw up 2 mL of the above solution (100 mg of vancomycin) and add 18 mL glucose 5% or sodium chloride 0.9% to make a final volume of 20 mL with a final concentration of 5 mg/mL. **<u>1g VIAL</u>** Add 20 mL of water for injection to the 1g powder for reconstitution to make a 50 mg/mL solution **Further Dilute:** Draw up 2 mL of the above solution (100 mg of vancomycin) and add 18 mL glucose 5% or sodium chloride 0.9% to make a final volume of 20 mL with a final concentration of 5 mg/mL. **<u>Special circumstances</u>** In special circumstances, e.g. fluid restricted infants, vancomycin can be diluted to 10 mg/mL, however this dilution increases the risk of infusion-related events (see adverse reactions).

Method		Interval
Corrected Gestational Age/Postmenstrual Age	**Postnatal Age**	
< 30^{+0} weeks	0–2 days	18 hourly
< 30^{+0} weeks	3+ days	12 hourly
30^{+0}–36^{+6} weeks	0–14 days	12 hourly
30^{+0}–36^{+6} weeks	15+ days	8 hourly
37^{+0}–44^{+6} weeks	0–7 days	12 hourly
37^{+0}–44^{+6} weeks	8+ days	8 hourly
≥ 45^{+0} weeks	0+ days	6 hourly

	500mg VIAL To prepare 10 mg/mL concentration: Add 10 mL of water for injection to the 500 mg vial to make a 50 mg/mL solution **Further Dilute:** Draw up 4 mL of the above solution (200 mg of vancomycin) and add 16 mL glucose 5% or sodium chloride 0.9% to make a final volume of 20 mL with a final concentration of 10 mg/mL. **1g VIAL** To prepare 10 mg/mL concentration: Add 20 mL of water for injection to the 1g vial to make a 50 mg/mL solution **Further Dilute:** Draw up 4 mL of the above solution (200 mg of vancomycin) and add 16 mL glucose 5% or sodium chloride 0.9% to make a final volume of 20 mL with a final concentration of 10 mg/mL.
Administration	IV infusion over ONE hour. Adequately flush the intravenous lines before and after administration of vancomycin.
Monitoring	Monitor renal function, full blood count, hearing function and serum vancomycin concentrations. **Measure trough vancomycin concentration immediately prior to 3rd dose with the exception of: (1)** <29^{+0} CGA weeks – before 2nd dose, (2) therapeutic hypothermia – before 2^{nd} dose and (3) renal impairment – before 2^{nd} dose, but refer to renal impairment section below. Check concentration prior to the 4th dose after any change in dose or frequency. Once target trough levels are reached, measure trough levels every 3 days prior to the dose. More frequent monitoring may be required as in following situations: in renal impairment, infants receiving other nephrotoxic drugs or in suspected severe sepsis. Target trough concentration: 10–20 mg/L (aim for higher trough level: 15–20 mg/L in suspected severe sepsis e.g., MRSA, bone infection, meningitis, endocarditis). If a peak concentration is required to guide dosing, perform this 1 hour after completion of infusion, and target a peak concentration 20-40 mg/L. [22] **Recommended adjustment based on trough concentration:** < 5 mg/L – increase total daily dose by 50–75% (i.e. 1.5-1.75 times)) by either increasing frequency (preferred) or increasing each dose. 5–9.9 mg/L – increase total daily dose by 25–50% (i.e. 1.25-1.5 times) by either increasing frequency (preferred) or increasing each dose. 10–20 mg/L – no change in dose required. 20.1–30 mg/L – decrease total daily dose by 10–30% (i.e. 0.9-0.7 times) by decreasing frequency (preferred) or decreasing each dose. > 30 mg/L – withhold dose. Repeat trough concentration 24 hourly until plasma concentration is 10–20 mg/L, then restart at a dose decreased by 50% (i.e. 0.5 times) by decreasing frequency (preferred) or decreasing each dose. **Example for adjusting dose by increasing / decreasing frequency:** Calculate current total daily dose (e.g. 15 mg 8 hourly = 45 mg/day). If trough <5 mg/L – Increase total daily dose by 1.5 times (i.e. 45 x 1.5 = 67.5 mg/day) and decide on achieving this total daily dose by either increasing the frequency or increasing the dose. : If trough 20.1–30 mg/L - Decrease total daily dose to 0.7 times (i.e. 45 x 0.7 = 31.5 mg/day) and decide on achieving this total daily dose by either decreasing the frequency or decreasing the dose. **Renal impairment** For infants with renal impairment, consider using an antibiotic without nephrotoxicity in consultation with an infectious diseases specialist. If vancomycin is used, perform a trough concentration before the 2nd dose, irrespective of corrected gestational age.
Contraindications	Known hypersensitivity to vancomycin.
Precautions	Use with caution in patients with renal impairment or those receiving other nephrotoxic, neurotoxic or ototoxic drugs.

Drug interactions	Neurotoxic and nephrotoxic drugs – concurrent use of these agents may contribute to the additive neurotoxic and nephrotoxic effects. Diuretics – potent diuretics (e.g., furosemide) may add to the ototoxic effect. Neuromuscular blocking agents (e.g. pancuronium, suxamethonium, vecuronium) – vancomycin may enhance neuromuscular blockade. Vancomycin may be combined with an aminoglycoside, cephalosporin or rifampicin for synergistic activity.
Adverse reactions	Infusion-related events: Rapid infusion may cause red man syndrome – a predominately histamine-mediated reaction with pruritus, tachycardia, hypotension and rash. It appears rapidly and usually dissipates in 30–60 minutes, but may persist for several hours. Increasing the infusion time usually eliminates the risk for subsequent doses. Anaphylactic reactions may occur. Severe reactions may require treatment with adrenaline (epinephrine), corticosteroids or oxygen. Phlebitis and tissue irritation and necrosis may occur, especially after extravasation. Intramuscular injection is not recommended. Neurotoxicity, ototoxicity and nephrotoxicity – these are more pronounced with the addition of other medications such as aminoglycosides or furosemide. Neutropenia and thrombocytopenia have been reported in adults. Risk is increased with prolonged therapy >1 week but they appear to be reversible when vancomycin is discontinued.
Compatibility	Fluids: Glucose 5%, glucose 10%, sodium chloride 0.9%. Y site: amino acid solutions and fat emulsions, aciclovir, adrenaline (epinephrine) hydrochloride, amifostine, amiodarone, anidulafungin, atracurium, caspofungin, cisatracurium, dobutamine, dopamine, dexmedetomidine, esmolol, filgrastim, fluconazole, gentamicin, granisetron, hydromorphone, insulin regular, labetalol, linezolid, magnesium sulfate, meropenem, midazolam, milrinone, morphine sulfate, mycophenolate mofetil, noradrenaline (norepinephrine), palonosetron, pancuronium, pethidine, potassium chloride, remifentanil, tigecycline, vecuronium, zidovudine.
Incompatibility	Fluids: No information. Y-site: albumin, aminophylline, azathioprine, beta-lactam antibiotics (eg. penicillins, cephalosporins), bivalirudin, calcium folinate, chloramphenicol, daptomycin, foscarnet, furosemide, ganciclovir, heparin sodium, indometacin, ketorolac, methylprednisolone sodium succinate, moxifloxacin, omeprazole, rocuronium, sodium bicarbonate, sodium valproate, streptokinase, urokinase.
Stability	Administer immediately, discard unused portion of reconstituted solution.
Storage	Store below 25°C. Protect from light.
Excipients	DBL Vancomycin Hydrochloride, Vancocin CP: Disodium acetate.
Special comments	Extravasation may cause tissue necrosis.
Evidence	Refer to full version.
Practice points	
References	Refer to full version.

VERSION/NUMBER:	**DATE**
Original: 1.0	**8/08/2015**
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1.1	**7/07/2016**
1.2	**12/12/2016**
1.3	**6/07/2017**
1.4	**10/08/2017**
2.0	**15/04/2017**
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