# Vancomycin – continuous infusion regimen 2019

## Newborn Use Only

<table>
<tr><td>Alert</td><td>The Antimicrobial Stewardship Team recommends this drug is listed under the following category: Restricted.<br>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.</td></tr>
<tr><td>Indication</td><td>Infections due to susceptible strains of the following organisms: Staphylococci (including MRSA), Streptococci, Enterococci, Diptheroids, Listeria monocytogenes, Actinomyces, Bacillus spp.</td></tr>
<tr><td>Action</td><td>Bactericidal agent which interferes with cell wall synthesis, inhibits RNA synthesis and alters plasma membrane function.</td></tr>
<tr><td>Drug Type</td><td>Glycopeptide antibiotic.</td></tr>
<tr><td>Trade Name</td><td>Vancocin CP, Vancomycin Hydrochloride DBL, Vancomycin Alphapharm, Vancomycin Sandoz Vycin.</td></tr>
<tr><td>Presentation</td><td>Vancomycin hydrochloride 500 mg vial<br>Vancomycin hydrochloride 1000 mg vial</td></tr>
<tr><td>Dosage / Interval</td><td>Loading dose 15 mg/kg over 1 hour, immediately followed by<br>Continuous infusion as per the table below:*
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<tr><th>Serum Creatinine (micromol/L)</th><th>Corrected gestational age (CGA)</th><th>Dose</th></tr>
<tr><td><40</td><td>≥40 weeks</td><td>2.1 mg/kg/hour (equivalent to 50 mg/kg/day)</td></tr>
<tr><td><40</td><td><40 weeks</td><td>1.7 mg/kg/hour (equivalent to 40 mg/kg/day)</td></tr>
<tr><td>40–60</td><td>All</td><td>1.25 mg/kg/hour (equivalent to 30 mg/kg/day)</td></tr>
<tr><td>>60</td><td>All</td><td>0.8 mg/kg/hour (equivalent to 20 mg/kg/day)</td></tr>
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E.g. 3 kg baby at 41 weeks corrected gestational age with serum Cr 37 = 2.1 mg/kg/hour x 3.0 kg = 6.3 mg/hour<br><br>Measure vancomycin concentration 24 hours (18–30 hours) and 48 hours after the start of infusion and then every 3 days. Adjust the dose as per the monitoring section.<br><br>Doctor's prescription order: Prescribe (1) loading dose on ONCE ONLY section of the medication chart and (2) infusion dose in mg/kg/hour on fluid chart.</td></tr>
<tr><td>Route</td><td>IV</td></tr>
<tr><td>Preparation/Dilution</td><td>Add 10 mL of water for injection to the 500 mg vial to make a 50 mg/mL solution. Then:<br><br><u>For 5 mg/mL strength (for peripheral lines):</u><br>Draw up 5 mL of 50 mg/mL solution (250 mg of vancomycin) and add 45 mL of glucose 5% or sodium chloride 0.9% to make a final volume of 50 mL with a final concentration of 5 mg/mL.<br><br><u>For 10 mg/mL strength (for central lines and fluid restricted infants):</u><br>Draw up 10 mL of 50 mg/mL solution (500 mg of vancomycin) and add 40 mL of glucose 5% or sodium chloride 0.9% to make a final volume of 50 mL with a final concentration of 10 mg/mL.</td></tr>
<tr><td>Administration</td><td>For Loading dose: IV infusion over ONE hour.<br>For Maintenance infusion: Continuous IV infusion. Change solution every 24 hours.</td></tr>
<tr><td>Monitoring</td><td>Monitor renal function, full blood count, hearing function and serum vancomycin concentrations.<br><br>Measure vancomycin concentration 24 hours (18–30 hours) after the start of infusion AND 24 hours after each change of infusion rate.<br><br>If 24 hour vancomycin concentration is 15–25 mg/L: Repeat steady state level at 48 hours then every 3 days; or earlier if:<br>(1) 10% change in body weight OR<br>(2) 25% change in serum creatinine OR<br>(3) age-related dose adjustment OR<br>(4) interruption in IV infusion OR<br>(5) infant receives indomethacin.<br><br>If vancomycin level <15 or >25 mg/L: Adjust dose using below calculation:</td></tr>
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| | Adjusted dose (mg/kg/hour) = last maintenance dose (mg/kg/hour) x (20 ÷ last vancomycin concentration)5<br>After dose adjustment, repeat vancomycin concentration after 24 hours until target concentrations are reached.<br>**Adjustment to > 4.2 mg/kg/hour (100mg/kg/day) should not be done without discussion with pharmacist and consultant.**<br><br>*For example, last dose was 2.1 mg/kg/hour and the last vancomycin concentration was 12 mg/L:*<br>*Adjusted dose = 2.1 mg/kg/hour x (20 mg/L ÷ 12 mg/L)*<br>*= 3.5 mg/kg/hour*<br><br>*For example, last dose was 2.1 mg/kg/hour and the last vancomycin concentration was 28 mg/L:*<br>*Adjusted dose = 2.1 mg/kg/hour x (20 mg/L ÷ 28 mg/L)*<br>*= 1.5 mg/kg/hour* |
| **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.<br>Diuretics – potent diuretics (e.g. furosemide [frusemide]) may add to the ototoxic effect.<br>Neuromuscular blocking agents (e.g. pancuronium, suxamethonium, vecuronium) – vancomycin may enhance neuromuscular blockade.<br>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.<br>Anaphylactic reactions may occur. Severe reactions may require treatment with adrenaline (epinephrine), corticosteroids and oxygen.<br>Phlebitis and tissue irritation with necrosis may occur, especially after extravasation.<br>Intramuscular injection is not recommended.<br>Neurotoxicity, ototoxicity and nephrotoxicity – these are more pronounced with the addition of other medications such as aminoglycosides or furosemide (frusemide).<br>Neutropenia and thrombocytopenia have been reported in adults; risk is increased with prolonged therapy >1 week and they appear to be reversible when vancomycin is discontinued. |
| **Compatibility** | Fluids: Glucose 5%, glucose 10%, sodium chloride 0.9%.<br><br>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** | Y-site: Albumin, aminophylline, azathioprine, beta-lactam antibiotics (e.g. penicillins, cephalosporins), bivalirudin, calcium folinate, chloramphenicol, daptomycin, foscarnet, furosemide (frusemide), 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.<br>Infusion solution is stable for 24 hours below 25°C. |
| **Storage** | Store below 25°C. Protect from light. |
| **Special Comments** | If IV infusion is interrupted frequently or for longer periods of time, recommend changing over to intermittent regimen.<br>In severe sepsis, if the IV infusion is interrupted for short duration (e.g. up to 4 hours), consider |

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| | giving the missed dose over an hour followed by the continuous infusion at the original rate. |
| **Evidence summary** | Refer to full version. |
| **References** | Refer to full version. |
| **Commentary** | This is the first time the consensus group has introduced a continuous infusion regimen for vancomycin after publication of a RCT comparing continuous and intermittent regimen in newborn infants (Pediatrics. 2019 Feb 1;143(2):e20182179).<br><br>A continuous regimen was reported to optimise achievement of steady state target concentrations with fewer dose adjustments and a lower total daily dose compared to an intermittent regimen. However, the participants' mean birth weight (2271 g), gestation at birth (34 weeks) and current weight (2549 g) were relatively higher than populations treated by many perinatal centres. However, there are practical issues in terms of intravenous access for continuous infusion in extremely premature infants. The consensus group considered that whilst continuous infusion has better pharmacokinetic efficacy the group is not able to recommend a preferred regimen.<br><br>In this revised version, monitoring section has been further improved: Vancomycin level is not a steady state at 24 hours. Half-life varies between 3.5 to 10 hours in newborns and is longer in renal impairment, PDA, indomethacin. Also, a level at 24 hours, then 3 days later as suggested in the previous version may miss some very high steady state levels which could occur after the 50 hour mark. Changes were made in this updated version to address this issue suggesting to measure at 24 hours, then 48 hours and then every 3 days. |

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**Authors Contribution**

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|---|---|
| Original author/s | David Osborn, Srinivas Bolisetty |
| Evidence Review - original | David Osborn |
| Expert review | Amanda Gwee, Tony Lai, Brendan McMullan, Alison Kesson, Hemalatha Varadhan |
| Nursing Review | Eszter Jozsa |
| Pharmacy Review | Jing Xiao, Michelle Jenkins, Cindy Chen |
| ANMF Group contributors | Nilkant Phad, Himanshu Popat |
| Final editing and review of the original | Ian Whyte |
| Electronic version | Cindy Chen, Ian Callander |
| Facilitator | Srinivas Bolisetty |