Alert
The Antimicrobial Stewardship Team recommends this drug is listed under the following category: restricted

Indication
Infections due to susceptible strains of the following organisms: Staphylococci (including MRSA), Streptococci, Enterococci, Diptheroids, Listeria monocytogenes, Lactobacilli, Actinomyces, Bacillus sp.

Action
Bactericidal agent which interferes with cell wall synthesis, inhibits RNA synthesis and alters plasma membrane function.

Drug Type
Glycopeptide antibiotic

Trade Name
Vancocin CP, Vancomycin Hydrochloride (DBL), Vancomycin Alphapharm, Vacomycin Sandoz

Presentation
Vancomycin Hydrochloride 500mg vial
Vancomycin Hydrochloride 1000mg vial

Dosage / Interval
Standard infections: 15mg/kg dosing interval as per table below

<table>
<thead>
<tr>
<th>Method</th>
<th>Interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corrected Gestational Age</td>
<td>Age</td>
</tr>
<tr>
<td>&lt; 30 weeks</td>
<td>0-14 days</td>
</tr>
<tr>
<td>&lt; 30 weeks</td>
<td>15+ days</td>
</tr>
<tr>
<td>30-36 weeks</td>
<td>0-14 days</td>
</tr>
<tr>
<td>30-36 weeks</td>
<td>15 + days</td>
</tr>
<tr>
<td>37-44 weeks</td>
<td>0-7 days</td>
</tr>
<tr>
<td>37-44 weeks</td>
<td>8 + days</td>
</tr>
<tr>
<td>≥ 45 weeks</td>
<td>0 +</td>
</tr>
</tbody>
</table>

Consider giving a loading dose of 20mg/kg/dose in suspected severe sepsis e.g. MRSA, bone infection, meningitis, endocarditis. However, data in neonates is limited.

Route
IV

Preparation/Dilution
Add 10mL of water for injection to the 500mg vial to make a 50mg/mL solution. Draw up 1mL (50mg) of vancomycin and add 9mL glucose 5% or sodium chloride 0.9% to make a final volume of 10mL with a final concentration of 5mg/mL

Administration
IV infusion over ONE hour.

Monitoring
Monitor renal function, full blood count, hearing function and serum vancomycin concentrations. Trough level: 10 to 20mg/L (higher trough level: 15 to 20mg/L in suspected severe sepsis e.g. MRSA, bone infection, meningitis, endocarditis)

Trough level should be taken within an hour prior to the:
2nd dose for 18 hourly dosing
4th dose for all other frequencies.

More frequent monitoring may be required in renal impairment, those receiving other nephrotoxic drugs or in suspected severe sepsis.

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
Beta-lactam antibiotics have been shown to be physically incompatible. The likelihood of precipitation increases with higher concentrations of vancomycin.
Neurotoxic and nephrotoxic drugs (e.g. gentamicin, amikacin, amphotericin B) – concurrent use of these agents may contribute to the additive neurotoxic and nephrotoxic effects.
Diuretics – potent diuretics (e.g. frusenide) may aggravate the ototoxic effects.
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 – erythema multiforme-like reaction with pruritis, tachycardia, hypotension and rash. It appears rapidly and dissipates in 30-60 minutes, but may persist for several hours. Increasing the infusion time usually eliminates the risk for subsequent doses.
Anaphylactoid reactions may occur. Severe reactions may require treatment with adrenaline, 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 frusemide.
Neutropenia and thrombocytopenia has been reported in adults; risk is increased with prolonged therapy > 1 week that appears to be reversible when vancomycin is discontinued.

Compatibility
Fluids: Glucose 5%, glucose 10%, sodium chloride 0.9%
Y site: Aciclovir, amifostine, amiodarone, anidulafungin, atracurium, caspofungin, cisatracurium, dexmedetomidine, esmolol, filgrastim, fluconazole, granisetron, hydromorphone, labetalol, linezolid, lorazepam, magnesium sulfate6, midazolam, morphine sulfate, mycophenolate mofetil, palonosetron, pancuronium, pethidine, remifentanil, tigecycline, vecuronium, zidovudine

Incompatibility
Fluids: No information
Drugs: Adrenaline hydrochloride, albumin, aminophylline, azathioprine, bivalirudin, calcium folinate, chloramphenicol, daptomycin, foscarnet, frusemide, ganciclovir, heparin sodium, indomethacin, 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.

Special Comments
Extravasation may cause tissue necrosis

Evidence summary
1. Effectiveness:
A 2 hospital crossover study comparing ampicillin versus penicillin combined with gentamicin in the empiric therapy of extremely low-birth weight neonates at risk of early onset sepsis showed similar effectiveness in change of antibiotics at 72 hours and/or 7-day all cause mortality. (11, 12)
A systematic review comparing the effectiveness and safety of penicillin or ampicillin-chloramphenicol versus third generation cephalosporin in patients with community-acquired suspected acute bacterial meningitis found 12 trials enrolling infants under 1 year of age. There were no significant differences between the groups in the risk of death, deafness, or treatment failure; there were significantly decreased risks of culture positivity of CSF after 10 to 48 hours and increases in the risk of diarrhea between the groups (RD 8%; 95% CI 3% to 13%) with third generation cephalosporin. (13)

2. Dose: There are no clinical trials comparing standard versus high dose ampicillin in neonates with sepsis or meningitis.
Clinical trials reporting effectiveness of regimens including ampicillin for meningitis reported use of daily doses of ampicillin >=200mg/kg/day. (13) Doses of ampicillin 200mg/kg/day result in adequate CSF concentrations for treatment of enterococcus and Listeria monocytogenes.(10, 14)

Recommendation:
When ampicillin is used in combination with an aminoglycoside for the treatment of meningitis, it is recommended that the dose be doubled from 50 to 100 mg/kg/dose. (Level of evidence III-2, Grade of recommendation B).

Level of evidence
Grade of recommendation*

*Level of evidence
Grade of recommendation

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# References

4. Paediatrics and Neofax online. Truven Health Analytics. 2013
10. Roberts JK. et al. (2014) Pharmacokinetics and Pharmacodynamics of Antibacterials, Antifungals, and Antivirals Used Most Frequently in Neonates and Infants; Clin Pharmacokinet, 53:584-610