

| <b>Alert</b>                 | High risk medicine. The Antimicrobial Stewardship Team recommends this drug is listed under the following category: Unrestricted.<br>Contains 48 mg of sodium per gram of cefazolin sodium.  |               |           |               |            |      |          |          |       |               |           |       |               |           |          |       |               |          |       |               |          |
|------------------------------|--|---------------|-----------|---------------|------------|------|----------|----------|-------|---------------|-----------|-------|---------------|-----------|----------|-------|---------------|----------|-------|---------------|----------|
| <b>Indication</b>            | Treatment of infections caused by susceptible organisms: <ul style="list-style-type: none"> <li>Gram positive bacteria Streptococci and Staphylococci including beta-lactamase producing Staphylococci</li> <li>Gram negative bacteria <i>Escherichia coli</i> and some <i>Klebsiella</i> species, provided these are reported susceptible to cefazolin).</li> </ul> Peri-operative prophylaxis (ANMF consensus)   |               |           |               |            |      |          |          |       |               |           |       |               |           |          |       |               |          |       |               |          |
| <b>Action</b>                | Bactericidal. Inhibits bacterial cell wall synthesis of actively dividing cells by binding to one or more penicillin binding proteins.   |               |           |               |            |      |          |          |       |               |           |       |               |           |          |       |               |          |       |               |          |
| <b>Drug type</b>             | Antibiotic, First generation cephalosporin.  |               |           |               |            |      |          |          |       |               |           |       |               |           |          |       |               |          |       |               |          |
| <b>Trade name</b>            | Cefazolin Sandoz, Cefazolin-AFT, Hospira Cefazolin, Kefzol, Cephazolin Alphapharm  |               |           |               |            |      |          |          |       |               |           |       |               |           |          |       |               |          |       |               |          |
| <b>Presentation</b>          | 1 g vial.  |               |           |               |            |      |          |          |       |               |           |       |               |           |          |       |               |          |       |               |          |
| <b>Dose</b>                  | <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th>Postnatal age</th> <th>Weight (g)</th> <th>Dose</th> <th>Interval</th> </tr> </thead> <tbody> <tr> <td rowspan="2" style="text-align: center;">&lt; 8 days</td> <td style="text-align: center;">&lt;2000</td> <td style="text-align: center;">25 mg/kg/dose</td> <td style="text-align: center;">12 hourly</td> </tr> <tr> <td style="text-align: center;">≥2000</td> <td style="text-align: center;">50 mg/kg/dose</td> <td style="text-align: center;">12 hourly</td> </tr> <tr> <td rowspan="2" style="text-align: center;">≥ 8 days</td> <td style="text-align: center;">&lt;2000</td> <td style="text-align: center;">25 mg/kg/dose</td> <td style="text-align: center;">8 hourly</td> </tr> <tr> <td style="text-align: center;">≥2000</td> <td style="text-align: center;">50 mg/kg/dose</td> <td style="text-align: center;">8 hourly</td> </tr> </tbody> </table> <p>For peri-operative prophylaxis: Duration is for 1-2 days. To discuss with surgeons/infectious diseases specialist.</p> |               |           | Postnatal age | Weight (g) | Dose | Interval | < 8 days | <2000 | 25 mg/kg/dose | 12 hourly | ≥2000 | 50 mg/kg/dose | 12 hourly | ≥ 8 days | <2000 | 25 mg/kg/dose | 8 hourly | ≥2000 | 50 mg/kg/dose | 8 hourly |
| Postnatal age                | Weight (g)   | Dose          | Interval  |               |            |      |          |          |       |               |           |       |               |           |          |       |               |          |       |               |          |
| < 8 days                     | <2000  | 25 mg/kg/dose | 12 hourly |               |            |      |          |          |       |               |           |       |               |           |          |       |               |          |       |               |          |
|                              | ≥2000  | 50 mg/kg/dose | 12 hourly |               |            |      |          |          |       |               |           |       |               |           |          |       |               |          |       |               |          |
| ≥ 8 days                     | <2000  | 25 mg/kg/dose | 8 hourly  |               |            |      |          |          |       |               |           |       |               |           |          |       |               |          |       |               |          |
|                              | ≥2000  | 50 mg/kg/dose | 8 hourly  |               |            |      |          |          |       |               |           |       |               |           |          |       |               |          |       |               |          |
| <b>Dose adjustment</b>       |  |               |           |               |            |      |          |          |       |               |           |       |               |           |          |       |               |          |       |               |          |
| <b>Maximum dose</b>          |  |               |           |               |            |      |          |          |       |               |           |       |               |           |          |       |               |          |       |               |          |
| <b>Total cumulative dose</b> |  |               |           |               |            |      |          |          |       |               |           |       |               |           |          |       |               |          |       |               |          |
| <b>Route</b>                 | IV infusion (preferable); IV bolus; IM   |               |           |               |            |      |          |          |       |               |           |       |               |           |          |       |               |          |       |               |          |
| <b>Preparation</b>           | <p><b>IV Infusion</b><br/>Add 9.5 mL water for injection to the 1 g vial to make 100 mg/mL solution<br/><b>FURTHER DILUTE</b><br/>Draw up 5 mL (500 mg of cefazolin) and add 15 mL of sodium chloride 0.9% to make a final volume of 20 mL with a final concentration of 25 mg/mL.</p> <p><b>IV bolus:</b> Add 9.5 mL water for injection to the 1 g vial to make a 100 mg/mL solution.</p> <p><b>IM:</b> Add 2.5 mL water for injection to the 1 g vial to make a 330 mg/mL solution.</p>   |               |           |               |            |      |          |          |       |               |           |       |               |           |          |       |               |          |       |               |          |
| <b>Administration</b>        | IV infusion: Infuse over 30 minutes (10-60 minutes).<br>IV bolus: Slow injection over 5 minutes.<br>IM: Inject deep into large muscle mass.  |               |           |               |            |      |          |          |       |               |           |       |               |           |          |       |               |          |       |               |          |
| <b>Monitoring</b>            | Serum concentrations are not routinely monitored.<br>Perform renal function, electrolytes and FBC during prolonged (> 10 days) therapy.  |               |           |               |            |      |          |          |       |               |           |       |               |           |          |       |               |          |       |               |          |
| <b>Contraindications</b>     | History of allergy to cephalosporins, anaphylaxis to penicillin or carbapenem.   |               |           |               |            |      |          |          |       |               |           |       |               |           |          |       |               |          |       |               |          |
| <b>Precautions</b>           | Sodium restriction — each gram of cefazolin contains 48.3 mg (2.1 mmol) sodium.<br>May increase risk of bleeding due to its effect on clotting factors.<br>Impaired renal function: consider reducing dose as seizures may occur if inappropriately high doses are administered.   |               |           |               |            |      |          |          |       |               |           |       |               |           |          |       |               |          |       |               |          |
| <b>Drug interactions</b>     | Administration with other drugs, particularly aminoglycosides may increase risk of nephrotoxicity.   |               |           |               |            |      |          |          |       |               |           |       |               |           |          |       |               |          |       |               |          |
| <b>Adverse reactions</b>     | Thrombophlebitis, pruritus, rash, diarrhoea, nausea, oral candidiasis, pseudomembranous colitis, vomiting, Stevens Johnson Syndrome, <i>Clostridium difficile</i> colitis, positive Coombs test, eosinophilia, leukopenia, neutropenia, thrombocytopenia, thrombocytosis, blood coagulation disorder, raised liver enzymes, candidiasis, raised urea, creatinine and renal failure.  |               |           |               |            |      |          |          |       |               |           |       |               |           |          |       |               |          |       |               |          |
| <b>Compatibility</b>         | <b>Fluids:</b> Glucose 5%, glucose 10%, glucose in sodium chloride solutions, Hartmann's, sodium chloride 0.9%, water for injections.  |               |           |               |            |      |          |          |       |               |           |       |               |           |          |       |               |          |       |               |          |

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|-------------------------|---|
|                         | <b>Y-site:</b> Aciclovir, amifostine, anidulafungin, atracurium, aztreonam, bivalirudin, dexmedetomidine, esmolol, filgrastim, fluconazole, foscarnet, granisetron, heparin sodium, linezolid, magnesium sulfate, midazolam, morphine sulfate, palonosetron, pancuronium, pethidine, remifentanyl, vecuronium.  |
| <b>Incompatibility</b>  | Fluids: No information<br>Drugs: Aminoglycosides – amikacin, gentamicin, tobramycin; ascorbic acid, azathioprine, calcium chloride, caspofungin, chlorpromazine, dobutamine, dolasetron, dopamine, erythromycin, ganciclovir, haloperidol lactate, hydralazine, mycophenolate mofetil, pentamidine, promethazine, rocuronium.   |
| <b>Stability</b>        | Stable for 24 hours below 25°C. However store at 2 to 8°C and use as soon as possible. Crystals may form if the solution is refrigerated. Redissolve by shaking the vial and warming in the hands.  |
| <b>Storage</b>          | Store below 25°C. Protect from light.   |
| <b>Excipients</b>       |   |
| <b>Special comments</b> | Poor penetration into cerebrospinal fluid therefore not suitable for infections of the CNS.<br>Renally excreted as unchanged drug. Not metabolised.<br>Half-life in neonates is 3 to 5 hours.<br>Cefazolin is highly bound to serum albumin –only the unbound cefazolin is pharmacologically active.<br>Water for injection is the preferred diluent. Crystals may form when cefazolin is reconstituted with sodium chloride 0.9% to a concentration of 330 mg/mL. The crystals formed are small and may be overlooked. Redissolve by warming the vial in hands until the solution is clear.  |
| <b>Evidence</b>         | The dosing regimen adopted by the consensus group is based on a neonatal pharmacokinetic model taking into account total and unbound cefazolin concentrations with saturable plasma protein binding. <sup>6</sup><br>A prospective validation of this dosing regimen is needed.   |
| <b>Practice points</b>  |   |
| <b>References</b>       | 1. Hey E. (Ed) [2003]. Neonatal Formulary 4th Edition. BMJ Publishing Group, London<br>2. MIMS Online Cited: 15/05/2015.<br>3. Micromedex® 2.0, (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: <a href="http://www.micromedexsolutions.com.acs.hcn.com.au">http://www.micromedexsolutions.com.acs.hcn.com.au</a> Cited 15/4/2015.<br>4. Australian Medicine Handbook 2015 (online). Adelaide: Australian Medicines Handbook Pty Ltd; 2015 January.<br>5. Antibiotic Expert Groups. Therapeutic guidelines: antibiotic. Version 15. Melbourne: Therapeutic Guidelines Limited; 2014.<br>6. De Cock R, Smits A, Allegoert K et al. Population pharmacokinetic modelling of total and unbound cefazolin plasma concentrations as a guide for dosing in preterm and term neonates. Journal of antimicrobial chemotherapy. Doi:10.1093/jac/dkt527 2013<br>7. Pacifici G. Pharmacokinetics of cephalosporins in the neonate: a review. Clinics 2011;66(7):1267-1274 |

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