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| Alert | The Antimicrobial Stewardship Team recommends this drug is listed under the following category: Restricted. |
| Indication | Treatment of systemic infection and meningitis caused by susceptible <i>Candida</i> species. Prophylaxis from <i>Candida</i> infection. |
| Action | Triazole antifungal which selectively inhibits fungal cytochrome P-450 sterol C-14 alpha demethylation. |
| Drug Type | Antifungal. |
| Trade Name | IV: Diflucan, Fluconazole Alphapharm, Aspen, Claris, Hexal, Sandoz. ORAL: Diflucan |
| Presentation | IV: 2 mg/mL injection ORAL: 50 mg/ 5mL powder for reconstitution |
| Dosage / Interval | <p>TREATMENT Loading dose: 25 mg/kg Maintenance dose: 12 mg/kg DAILY to start 24 hours after loading dose.</p> <p>The regimen without a loading dose may take up to 5 days to reach steady state. Steady state can be reached in 2 days if a loading dose is used.</p> <p>PROPHYLAXIS* 6 mg/kg TWICE per week</p> <p>*Fluconazole prophylaxis may be considered in high risk infants following completion of treatment for <i>Candida</i> sepsis but still carrying risk of recurrence- e.g., presence of indwelling catheters and ongoing skin thrush.</p> |
| Route | IV, Oral |
| Preparation/Dilution | IV: Administer 2 mg/mL injection –no dilution necessary. Oral: Powder normally reconstituted by Pharmacy. If supplied as dry powder reconstitute using water for injection with the volume specified on the bottle. |
| Administration | IV: Infusion over 30 minutes via a syringe pump. Oral: Can be given with feeds. Shake reconstituted bottle well before drawing up dose. |
| Monitoring | Measure serum creatinine prior to starting therapy. Monitor liver function, renal function and full blood count. |
| Contraindications | Cardiac rhythm problems– may increase QT interval. Hypersensitivity to fluconazole or other constituents. Concurrent therapy with other drugs known to prolong the QT interval and those drugs which are metabolised via the enzyme CYP3A4 e.g., cisapride, erythromycin. |
| Precautions | Consider extending dose interval to 48 hourly if creatinine > 115 micromol/L. Use with caution in hepatic impairment. May precipitate or worsen hyperbilirubinaemia, use with caution. May increase QT interval. |
| Drug Interactions | Erythromycin: Concurrent use increases the risk of cardiotoxicity (prolonged QT interval, torsades des pointes) therefore avoid combination. Barbiturates, caffeine, benzodiazepines and phenytoin: Serum concentrations increased by fluconazole, consider dose reduction and therapeutic drug monitoring. Hydrochlorothiazide: Increases fluconazole serum concentration, consider dose reduction of fluconazole. Zidovudine: Concentrations are increased by fluconazole; monitor for adverse reactions (anaemia, neutropenia) and extend dose interval. Cisapride: May precipitate arrhythmias, therefore contraindicated. |

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| Adverse Reactions | Rare: Rash, elevated LFTs, leucopenia including neutropenia and agranulocytosis and thrombocytopenia. |
| Compatibility | Fluids: Glucose 5%, glucose 10%, sodium chloride 0.9% Y-Site: Amino acid solutions, aciclovir, amifostine, amikacin, aminophylline, amiodarone, anidulafungin, aztreonam, benzotropine, bivalirudin, calcium folinate, ceftaxime, ceftazidime, ceftazidime fosamil, cefazolin, chlorpromazine, cisatracurium, dexamethasone, dexmedetomidine, dobutamine, dopamine, droperidol, filgrastim, foscarnet, ganciclovir, gentamicin, glyceryl trinitrate, granisetron, heparin sodium, linezolid, metoclopramide, metronidazole, midazolam, morphine sulfate, pancuronium, pethidine, piperacillin-tazobactam (EDTA-free), promethazine, ranitidine, remifentanyl, ticarcillin-clavulanate, tacrolimus, tigecycline, tobramycin, vancomycin, vecuronium, zidovudine. |
| Incompatibility | Y-site: Ampicillin, calcium gluconate, cefotaxime, ceftazidime, ceftriaxone, chloramphenicol, clindamycin, digoxin, frusemide, imipenem-cilastatin, pentamidine. |
| Stability | Vials: Discard remaining contents after use. Oral suspension: Discarded 14 days after reconstitution. |
| Storage | Vial and powder for reconstitution: Store below 25°C Reconstituted suspension: Store between 5–30°C |
| Special Comments | IV and oral doses are equivalent. |
| Evidence summary | Treatment dose: 12 mg/kg 24 hourly supported by pharmacokinetic data and Monte Carlo simulations (1,2; Grade B). Loading dose: 25 mg/kg loading dose is shown in Monte Carlo simulations to achieve target AUC by day 2 (2; Grade B). Post-treatment prophylaxis – expert opinion by Infectious Disease members of the Neomed Group. |
| References | 1. Wade KC. et al. (2008) Population Pharmacokinetics of Fluconazole in Young Infants, <i>Antimicrobial Agents and Chemotherapy</i> , vol.52; 11, p. 4043–4049. 2. Wade KC. et al. (2009) Fluconazole Dosing for the Prevention or Treatment of Invasive Candidiasis in Young Infants, <i>The Paediatric Infectious Disease Journal</i> , vol. 28; 8, 717–723. 3. Saxen H. et al.(1993) Pharmacokinetics of fluconazole in very low birth weight infants during the first two weeks of life, <i>Clinical Pharmacology & Therapeutics</i> , vol. 53; 3, 269-277. 4. Wenzl TG. et al. (1998) Pharmacokinetics of oral fluconazole in premature infants, <i>Eur J Pediatr</i> , 157:661-662. 5. Nahata MC, Tallian KB, Force RW. Pharmacokinetics of fluconazole in young infants. <i>Eur J Drug Metab Pharmacokinet</i> . 1999;24(2):155–157. 6. Takemoto CK et al. (2013) <i>Pediatric & Neonatal Dosage Handbook 20th Edition</i> , page 795-798 7. Trissel's IV Compatibility, accessed 04/08/2015 via Micromedex 2.0 8. Society of Hospital Pharmacists of Australia (2015) <i>Australian Injectable Drugs Handbook 6th Edition</i> , Fluconazole Monograph . 9. Young T.E. & Mangum B. (2011) <i>Neofax 2011</i> , page 42. 10. MIMs Product Information (2012) Fluconazole Sandoz Injection Product Information, Sandoz. 11. Neofax accessed on www.neofax.micromedex.solutions.com on 29 th July 2015. |

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