SydPath
ST VINCENT'S PATHOLOGY

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FLUCONAZOLE DRUG MEASUREMENT INFORMATION SHEET

<table>
<tr><td>Fluconazole</td><td>- Bis-triazole antifungal agent.
- Active against susceptible strains of Candida (variable activity against C. glabrata), Cryptococcus, dermatophytes and some dimorphic fungi.
- Inactive against C. krusei, most filamentous fungi, including Aspergillus spp. Fusarium spp.</td></tr>
<tr><td>When to consider TDM</td><td>Treatment of systemic infection, clinically unstable patients or patients receiving renal replacement therapy as can have altered dose-exposure relationship.</td></tr>
<tr><td>Pharmacokinetics (may be altered in critical illness and organ dysfunction)</td><td><table>
<tr><td>Absorption</td><td>Oral: >90%</td></tr>
<tr><td>Protein binding</td><td>11-12%</td></tr>
<tr><td>Clearance</td><td>Metabolism: minor; 11% Renal:80% as unchanged drug</td></tr>
<tr><td>Elimination t½</td><td>30 hours (range 20-50 hours)</td></tr>
<tr><td>Time to steady state</td><td>5 to 7 days can be achieved earlier if given loading dose</td></tr>
</table></td></tr>
<tr><td>Sample Collection Time</td><td>After the fifth dose or at steady state: Trough sample
Several samples throughout dosing interval to estimate AUC (thereby AUC/MIC ratio) may be reasonable: e.g. sampling at 1, 4, and 24h.</td></tr>
<tr><td>Requesting and Collection</td><td>Collect 4 mL in a purple top (EDTA) tube (no gel separator). Important information required on request form: 1) Time and date of last dose 2) Time since last dose change/commencement 3) Time of blood sample collection 4) Dosing regimen.</td></tr>
<tr><td>Handling and Transport</td><td>Sample must be delivered to laboratory within 1 hour of collection. If not delivered to the lab within 2 hours of collection, centrifuge, separate plasma and freeze within 3 hours of collection.</td></tr>
<tr><td>Availability</td><td>Test generally performed twice a week. Specific days and timing should be confirmed with SydPath.</td></tr>
<tr><td>Reference Intervals</td><td>Suggested Therapeutic Targets
Trough: > 2 mg/L for sensitive organisms.
NOTE: Most evidence suggests the use of AUC/MIC as the parameter most predictive of fluconazole efficacy. 24h AUC/MIC varies depending on MIC susceptibility testing methodology: >25 (CLSI[a]) or >100 (EUCAST[b]): associated with higher treatment success. - SydPath currently uses EUCAST method.
Toxic Range: Not well defined.</td></tr>
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Contact	Patient Results: (02) 8382 9100 Further information: www.sydpath.com.au - Test Database
Instructions for Referring laboratories	Centrifuge, separate plasma within 3 hours of collection, store and transport plasma frozen.
Document Approval	07/2017
References	[a] Clinical & Laboratory Standards Institute [b] European Committee On Antimicrobial Susceptibility Testing 1. Goodwin ML, Drew RH. Antifungal serum concentration monitoring: an update. J Antimicrob Chemother. 2008;61:17-25 2. Ashbee HR, Barnes RA et al. Therapeutic drug monitoring (TDM) of antifungal agents: guidelines from the British Society for Medical Mycology. J Antimicrob Chemother. 2014;69(5):1162-76. 3. Micromedex Solutions [Database]. Greenwood Village, Colorado: Truven Health Analytics 2017. Available from: www.micromedexsolutions.com.