SydPath
ST VINCENT'S PATHOLOGY

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VORICONAZOLE DRUG MEASUREMENT

INFORMATION SHEET

<table>
<tr><td>Voriconazole</td><td>- Broad-spectrum, 2nd generation triazole antifungal.
- Active against most Candida spp including fluconazole-resistant C. glabrata and C. krusei. Other yeasts and moulds including Aspergillus spp., Scedosporium sp. and Fusarium spp.</td></tr>
<tr><td>When to consider TDM</td><td>In all patients receiving voriconazole due to unpredictable, saturable kinetics and CYP2C19 genetic polymorphisms. TDM should be done regularly throughout treatment course. Consider TDM when starting or stopping interacting drugs.</td></tr>
<tr><td>Pharmacokinetics (may be altered in critical illness and organ dysfunction)</td><td>
<table>
<tr><td>Absorption</td><td>Oral: 65-96 %</td></tr>
<tr><td>Protein binding</td><td>58 %</td></tr>
<tr><td>Clearance</td><td>Clearance decreases at higher doses due to saturable metabolism.
<u>Metabolism:</u>
- Hepatic – extensive
- Saturable metabolism via CYP 2C19 (major), 2C9 and 3A4.
- Also inhibits CYP3A4, 2C19 and 2C9 activity. (May have clinically relevant drug-drug interactions)
<u>Renal:</u>
<2% unchanged</td></tr>
<tr><td>Elimination t½</td><td>Variable, dose dependent due to saturable pharmacokinetics. That is, dose increases lead to more than proportional increases in concentration.</td></tr>
<tr><td>Time to steady state</td><td>Dose dependent but may be achieved earlier if given loading dose.</td></tr>
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<tr><td>Sample Collection Time</td><td>Collect samples at steady state: Trough sample
* Initial sampling within first 2-5 days of therapy, however may not be at steady state, therefore repeated sampling may be required within 2-5 days.</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>
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Availability	Test generally performed 3 days a week. Specific days and timing should be confirmed with SydPath.
Reference Intervals	**Suggested Therapeutic Targets** [Prophylaxis & treatment]: Trough: >1 mg/L **Toxic Range:** Trough: >4-6 mg/L NOTE: A higher target (e.g. 2 mg/L) should be used if there is disease with poor prognosis (e.g. CNS infection, extensive disease, disseminated infection). A trough concentration of <4-6 mg/L is recommended to minimise drug-related toxicity. Note higher probability of toxicity with higher concentrations.
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	1. 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. 2. WB Park, N-H Kim, et al. The effect of therapeutic drug monitoring on safety and efficacy of voriconazole in invasive fungal infections: a randomized controlled trial. Clin Infect Dis. 2012 Oct; 55(8): 1080–1087 3. Klepser ME, Malone D, et al. Evaluation of Voriconazole Pharmacodynamics Using Time-Kill Methodology. Antimicrobial Agents and Chemotherapy. 2000;44(7):1917-1920. 4. Micromedex Solutions [Database]. Greenwood Village, Colorado: Truven Health Analytics 2017. Available from: www.micromedexsolutions.com. 5. Product Information: VFEND(R) IV injection, oral tablets, suspension, voriconazole IV injection, oral tablets, solution. Roerig, New York, NY, 2008