

HOSPITAL							Pharmacy Ref No:		
CLINICAL PHARMACOKINETICS SERVICE									
Antifungal Therapeutic Drug Monitoring (TDM) Request Form							Date Received :		
							Time Received :		
PATIENT PROFILE									
Name:			Race:			Ward/Unit:			
Gender: <input type="checkbox"/> M <input type="checkbox"/> F			Weight (kg):			IC:			
Age:			Height (cm):			DOA:			
CLINICAL SUMMARY AND DIAGNOSIS									
LATEST LAB RESULTS					CONCURRENT MEDICATIONS				
Parameters		Date	Results (unit)						
Hb / WBC / Platelet									
Albumin									
Serum Creatinine									
ALT / AST / ALP / Bilirubin									
CRP									
Fungal Biomarkers (if available)									
Culture & Sensitivity (specify MIC if available)									
SAMPLING DETAILS									
Sampling indication : <input type="checkbox"/> After dose initiation <input type="checkbox"/> Subsequent dose adjustment									
Drug Analysis (Tick <input type="checkbox"/> where appropriate)	Checklist for TDM (Tick <input type="checkbox"/> where appropriate)	Current Dose Regimen	Antifungal Initiation		Last Dose Given		Blood Sampling		
			Date	Time	Date	Time	Date	Time	
Voriconazole	NOT INDICATED <input checked="" type="checkbox"/> Short term prophylaxis (≤ 2 weeks)	LD: MD:							
Itraconazole	CONSIDER IN: <input type="checkbox"/> Difficult to treat invasive fungal infection / Deep seated infection <input type="checkbox"/> Poor clinical response	LD: MD:							
Posaconazole	<input type="checkbox"/> Suspected toxicity <input type="checkbox"/> Obesity (BMI >30 kg/m ²) <input type="checkbox"/> Concern with gastrointestinal absorption <input type="checkbox"/> Significant drug interactions (please specify):	LD: MD:							
Flucytosine	<input type="checkbox"/> Renal impairment (flucytosine only)	LD: MD:							
Isavuconazole	Routine TDM Is Not Indicated CONSIDER IN (Definitive therapy only): <input type="checkbox"/> Poor clinical response <input type="checkbox"/> Obesity (BMI >30 kg/m ²) <input type="checkbox"/> Concern with gastrointestinal absorption <input type="checkbox"/> Significant drug interactions (please specify):	LD: MD:							
REFER TO TDM SERUM SAMPLING GUIDELINES (refer back page)									
Requested by: (to be signed only by <u>ID Physician / Hematologist / Intensivist / Anaesthesiologist</u>)									
Doctor's Signature & Stamp: _____			Contact/Ext No: _____			Date: _____			
Drug Analysis	Result	Therapeutic Range	Scientific officer: Signature and Stamp:						
			Date: _____						
Pharmacist's Assessment & Recommendation :									
Pharmacist's signature & stamp									
Informed : DR / SN on atam/pm									

TDM SERUM SAMPLING GUIDE

DRUG	STEADY STATE (Time to monitor plasma concentrations)	SAMPLING TIME	THERAPEUTIC RANGE	Threshold for toxicity	Tube*
VORICONAZOLE	<p>After dose initiation: With LD: at least day 3 – 5 Without LD: at least day 5 – 8</p> <p>After dose adjustment or IV ↔ Oral switch: At least day 5 – 8</p> <p>Consider early sampling: In cases of worsening clinical condition or liver cirrhosis: after 3 – 5 days of dose adjustment</p>	<p>Trough: Within 30 minutes before next dose</p>	<p>Prophylaxis: ≥ 1 mg/L</p> <p>Treatment: ≥ 1 mg/L (≥ 2 mg/L for Aspergillosis, CNS infection or deep-seated infection)</p>	<p>> 4 mg/L** (Asian – mainly Japanese population)</p> <p>> 5.5 mg/L (non-Asian)</p> <p>** Given the genetic diversity of the Malaysian population, use the lower threshold with clinical judgment.</p>	
ITRACONAZOLE	<p>After dose initiation: With LD: at least day 6 – 8 Without LD: at least day 11 – 15</p> <p>After dose adjustment: At least day 11 – 15</p>	<p>Trough: Within 30 minutes before next dose</p>	<p>Prophylaxis ITZ only: ≥ 0.5 mg/L ITZ + OH-ITZ: ≥ 1 mg/L</p> <p>Treatment ITZ only: ≥ 1 mg/L ITZ + OH-ITZ: ≥ 2 mg/L</p>	<p>ITZ Only > 4 mg/L</p> <p>ITZ + OH-ITZ > 5 mg/L</p>	
POSACONAZOLE	<p>After dose initiation: With LD: at least day 6 Without LD: at least day 8 – 11</p> <p>After dose adjustment: At least day 8 – 11</p>	<p>Trough: Within 30 minutes before next dose</p>	<p>Prophylaxis: ≥ 0.5 mg/L</p> <p>Treatment: ≥ 1.25 mg/L</p> <p>Trough/MIC ratio: 5 – 8 (Aspergillus spp.)</p>	> 3.75 mg/L	
FLUCYTOSINE	At the 4th – 6th dose after initiation or dose adjustment	<p>Trough: Within 30 minutes before next dose</p> <p>Peak: 2 hours after oral dose (Consider if trough < 25 mg/L)</p>	<p>Trough: 25 – 50 mg/L</p> <p>Peak: Cryptococcal disease: 30 – 80 mg/L Other invasive fungal infections: 40 – 60 mg/L</p>	<p>Trough: No established toxicodynamic threshold</p> <p>Peak: ≥ 100 mg/L</p>	
ISAVUCONAZOLE <i>(Routine TDM is not indicated)</i>	<p>After dose initiation: With LD: at least day 6 – 8 Without LD: at least day 11 – 15</p> <p>After dose adjustment: At least day 11 – 15</p>	<p>Trough: Within 30 minutes before next dose</p>	<p>Trough: ≥ 1 – 2 mg/L</p>	> 5 mg/L	

! *IMPORTANT:
Send blood sample to pathology lab WITHIN 2 HOURS of collection for centrifugation.

For laboratory use:

Sample stability after centrifuge (Serum):

- 15 - 30°C: 1 day
- 2 - 8°C: 7 days
- < -18°C: 90 days

References:

1) HKL Antifungal Pharmacokinetic Guide 2025. 2) Instruction manual of Antimycotics in Serum / Plasma, RECIPE Chemicals+Instruments GmbH. 3) Zhang S et al. Development and validation of a high-performance liquid chromatographic assay for the determination of fluconazole in human whole blood using solid phase extraction. 4) Ther Drug Monit. 2008 Jun;30(3):314-9, Ganesh S et al. Development and validation of a volumetric absorptive microsampling assay for analysis of voriconazole and voriconazole N-oxide in human whole blood. Chromb (2018). 5) Flucytosine by Mass spectrometry, Serum/Plasma | ARUP Laboratories Test Directory. (n.d.). <https://ltd.aruplab.com/Tests/Pub/3018708>. 6) Itraconazole, serum - Laboratory Test Directory | South & West. (n.d.). <https://corewellhealth.testcatalog.org/show/LAB10010>. 7) Posaconazole, quantitative by LC-MS/MS | ARUP Laboratories Test Directory. (n.d.). <https://ltd.aruplab.com/Tests/Pub/2001739>.

LD: Loading dose; ITZ: Itraconazole; OH-ITZ: Hydroxyitraconazole