RECOMMENDED THERAPEUTIC DRUG MONITORING (TDM) FOR SELECT ANTIFUNGAL AGENTS IN ADULT PATIENTS*
DUKE UNIVERSITY HEALTH SYSTEM (DUHS)

General Antifungal Considerations & Recommendations

- The table below is intended to provide general guidance and **should NOT** replace clinical judgement.
- Prior to dosing adjustment, consider the following:
  - Medication adherence
  - Drug formulation
  - Drug interactions
  - Gut absorption
  - IV incompatibilities (*e.g.* IV posaconazole; see here for specific examples)
  - Presence of hypermetabolic state (*e.g.* extensive burn injuries)
- For individualized dose adjustment recommendations, please feel free to page the covering pharmacist or ASET pharmacist at 970-6666.

Drug name	DUHS Formulations	Timing¥	Target Concentration	Recommended Dose Adjustments	Notes
Azoles					
Posaconazole	Delayed Release (DR) tablet (100 mg) (preferred oral formulation) Oral suspension (40 mg/mL) Intravenous	5-7 days **Type:** trough (immediately prior to dose) Turnaround time 3-5 business days (send-out lab)	**Prophylaxis:** ≥ 0.7 mcg/mL **Treatment:** ≥ 1 mcg/mL (may consider ≥ 1.25 mcg/mL in select clinical cases) **Toxicity Threshold:** upper limit not established* *posaconazole-induced pseudohyperaldosteronism (PIPH) has been reported at higher troughs (*i.e.* >3-4 mcg/mL)	**< 0.7 mcg/mL (prophylaxis) or < 1.0 mcg/mL (or < 1.25 mcg/mL) (treatment)** • **DR tablet/IV:** increase daily dose by 100 mg and re-check in 5-7 days. Larger dose increases may be necessary in patients with concentration < 0.5 mcg/mL. • **Oral Suspension:** increase daily dose by 200-400 mg and re-check in 5-7 days (dose increases above 400 mg BID not recommended – consult ID pharmacist) **> 3 mcg/mL with PIPH (unless**	• **DR tablets:** preferred over suspension due to superior oral absorption. Should not be crushed • **IV:** requires a central line for administration. Contains cyclodextrin (which may accumulate in renal insufficiency) • **Suspension:** max individual dose is 400 mg due to saturable kinetics • Cyclodextrin is removed via HD and CRRT • If PIPH persists despite lower dose, consider switching azoles or symptom management (potassium repletion, blood

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Drug name	DUHS Formulations	Timing¥	Target Concentration	Recommended Dose Adjustments	Notes
				specified by ID consult team) • **DR tablet**: reduce daily dose by 100 mg and re-check in 5-7 days • **Oral Suspension:** reduce daily dose by 200 mg and re-check in 5-7 days	pressure management, and addition of an aldosterone antagonist)
Voriconazole	Tablets (50 mg, 200mg) Oral suspension (40mg/mL) Intravenous	5-7 days **Type:** trough (immediately prior to dose) Turnaround time 48 hours (run in-house)	**Prophylaxis:** ≥ 1 to ≤ 5.5 mcg/mL **Treatment:** ≥1 to ≤ 5.5 mcg/mL (Note: troughs >2 mcg/mL may be considered for select patients guided by ID consult team)	**< 1 mcg/mL:** increase daily dose by 50-100 mg and re-check in 5-7 days. Larger dose increases may be necessary in select patients (*e.g.* hypermetabolic states) **> 5.5 mcg/mL:** consider holding 1-2 doses and restarting at lower dose (decrease daily dose by 50-100 mg); recheck in 5-7 days	• High intra-patient PK variability due to polymorphisms in CYP2C19; nonlinear PK in adults • Take tablets/suspension on an empty stomach • Use adjusted body weight if obese • IV contains cyclodextrin (which may accumulate in renal insufficiency) • Cyclodextrin is removed via HD and CRRT • Visual disturbances or hallucinations may occur with higher exposure
Isavuconazole	Capsule (186 mg) Intravenous	Optimal population and timing for TDM not established; 5-7 days in select cases **Type:** trough (immediately prior to dose) Turnaround time 3-5 business days (send-out lab)	**Prophylaxis/Treatment:** not established; consider ≥1 mcg/mL in select cases **Toxicity Threshold:** not established	Not established if <1 mcg/mL consider increasing dose by 186 mg (1 capsule)	• IV can be given via a peripheral or central line (infuse with an in-line filter) • Consider further discussion with ID if concern for hypo or hyper metabolic state • Limited data exists for efficacy and toxicity thresholds. TDM may be warranted in select cases guided by ID consult team

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Itraconazole	Oral Capsule (100 mg) Oral Solution (10 mg/mL)	≥ 7 days **Type:** trough (immediately prior to dose) Turnaround time 3-5 business days (send-out lab)	**Prophylaxis:** ≥ 0.5 mcg/mL **Treatment:** ≥ 1 mcg/mL **Threshold for Toxicity:** Not established	**< 0.5 mcg/mL (prophylaxis) or** **< 1 mcg/mL (treatment):** Increase total daily dose by 100-200 mg	• Oral solution: higher bioavailability compared to the capsule. Administer on an empty stomach. Avoid using > 400 mg/dose. Divided dosing is recommended to improve absorption • Oral capsule: administer with full meal
Pyrimidines					
Flucytosine	Capsule (250 mg, 500 mg) Oral suspension (10 mg/mL)	Day 3 **Type:** peak (2 hours after dose) Turnaround time 3-5 business days (send-out lab)	**Cryptococcal Infections:** 30-80 mcg/mL **Candida Meningitis:** 40-60 mcg/mL **Toxicity Threshold:** >100 mcg/mL Concentrations > 100 mcg/mL associated with myelosuppression and hepatotoxicity	**Subtherapeutic by indication:** Increase total daily dose. Changes in serum concentration are proportional to dose adjustments **> 100 mcg/mL:** Decrease total daily dose. Changes in serum concentration are proportional to dose adjustments. Consider holding 1-2 doses and restarting at lower dose/interval if serum concentration > 150 mcg/mL	• Renal insufficiency: requires dose adjustment • Once target concentration established, repeat serum concentration monitoring unnecessary unless concern for toxicity or changing renal function leading to dose changes • Obese patients: use IBW

¥ after drug initiation and/or subsequent dose changes

*amphotericin B (polyene) and fluconazole (azole) are not recommended for routine TDM

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