Supplementary table 1: Pharmacology, common side effects and interactions for triazole antifungal agents with activity against *Aspergillus* spp.

	Itraconazole	Voriconazole	Posaconazole	Isavuconazole
Formulations	Capsules 100mg Solution 50mg/5ml	Tablets 200mg and 50mg Suspension 40mg/ml Injection 200mg	Tablets 100mg Suspension 40mg/ml Injection 300mg	Capsules 100mg Injection 200mg concentrate
Dose[a]	Oral 200mg BD <50kg consider 100mg BD	>50kg 200mg BD; 40-50kg 150mg BD <40kg 100mg BD IV: 6mg/kg BD 2 doses 4mg/kg BD	Oral /IV: 300mg OD <50kg consider 200mg OD	Oral/IV: 200mg OD
Absorption	Capsule: poor absorption, take with food or acidic drink[b] Liquid: better absorption, take on an empty stomach Peak levels at 2.5 hours	96% bioavailability Take on an empty stomach Peak levels at 1-2 hours,	Tablets: take with or without food, peak levels at 4-5 hours; Liquid: poor absorption, peak levels at 3 hours, take with high fat food	98% bioavailable Not affected by food Peak levels at 2-3 hours
Route of elimination	Hepatic via CYP3A4	Hepatic via CYP2C19, CYP2C9 and CYP3A4	Hepatic via uridine diphosphate-glucuronosyltransferases	Hepatic via CYP3A4, CYP3A5 and uridine diphosphate-glucuronosyltransferases
Half life	40 hours Non-linear pharmacokinetics	6 hours Non-linear pharmacokinetics	29 hours Linear kinetics	110 hours Linear kinetics
Main adverse effects	Gastrointestinal symptoms Oedema Heart failure Hypertension Prolonged QTc Peripheral neuropathy Hepatotoxicity Adrenal suppression Pseudo hyperaldosteronism	Gastrointestinal symptoms Phototoxicity Visual disturbance Hallucinations Hepatotoxicity Peripheral neuropathy Prolonged QTc Hyponatraemia Hypokalaemia	Gastrointestinal symptoms Oedema Heart failure Hypertension Prolonged QTc Peripheral neuropathy Hepatotoxicity Adrenal suppression Pseudo hyperaldosteronism	Gastrointestinal symptoms Peripheral neuropathy Shortened QTc Hepatotoxicity Hypokalaemia
Therapeutic drug level monitoring				
Therapeutic level	Depends on test used	1 – 5.5mg/L	1 - 3.75mg/L	Aim >1mg/L, preferably 2-4mg/L
Timing of levels	Trough preferable but random level acceptable	Trough	Trough preferable but random level acceptable	Trough preferable but random level acceptable
Frequency	2 to 4 weeks after starting therapy, then 3 months, then minimum 6 monthly (12 monthly for posaconazole) Plus after dose or formulation changes, or interacting medicines started or stopped			Not routinely recommended
Maximum dose	Titrate up to 300mg BD[c].	Titrate up to 350mg BD[c]	Titrate up to 400mg/day (tablets)[c,d]. Daily dose >300mg can use 2 divided doses	200mg OD[e]
Adverse effects monitoring regimen				
LFTs, U+Es	Baseline; then 2 to 4 weeks after starting or an increase in dose; then minimum annually; more frequently if high-risk of hepatotoxicity			

ECG	Baseline; then repeat at 2 to 4 weeks after starting if baseline ECG has prolonged QTc or taking another QTc prolonging medication or other risk factors			Baseline On starting medication that shortens QTc
Skin assessment	Not necessary	Each clinic visit (phototoxicity, SCCs)	Not necessary	Not necessary
Blood pressure	Clinic visits	Not necessary	Clinic visits	Not necessary
Cortisol	Annually, particularly for patients on long term inhaled or oral corticosteroids or taking multiple courses of oral corticosteroids			
Interactions				
Liver enzyme effects	Potent CYP3A4 inhibitor p-glycoprotein inhibitor	Potent CYP3A4, CYP2C19, CYP2C9 inhibitor	Potent CYP3A4 inhibitor	Moderate CYP3A4/5 inhibitor
Statins	Switch to pravastatin or rosuvastatin (not metabolised by CYP enzymes)			No significant interactions
Antacids / gastric acid suppression medication	Avoid if possible, or separate timing of administration	Halve the dose of omeprazole if taking 40+mg	Avoid if possible or monitor levels closely if on liquid form Tablets not affected	No significant interactions
Drugs affecting QTc	Monitor ECG if starting medication that can prolong QTc (eg macrolides, quinolones, citalopram)			Monitor ECG if on medication that can shorten QTc (eg nicorandil, rufinamide)
Corticosteroids	• Consider 50% dose reductions for - fluticasone, budesonide, ciclesonide, mometasone, dexamethasone, methylprednisolone, triamcinolone • No dose adjustment needed but monitor for side effects – beclomethasone, prednisolone, hydrocortisone			Clinical relevance unknown.
Immunosuppressives	Ciclosporin, tacrolimus, sirolimus and everolimus need close therapeutic monitoring (metabolised by CYP3A4)			
CFTR modulators	Consider dose adjustments according to manufacturers guidance for Ivacaftor, tezacaftor and elexacaftor			
Other	Drug metabolising enzymes inhibitors (eg ritonavir) or inducers (eg rifampicin, carbamazepine) require close monitoring of triazole levels			
Anticoagulants				
Warfarin	Inhibit warfarin metabolism, monitor INR closely			
Rivaroxaban, Apixaban	Contraindicated - levels increased			Use with caution
Edoxaban	Reduce to 30mg	No interaction	No dose reduction, monitor for increased bleeding risk	No dose reduction, monitor for increased bleeding risk
Dabigatran	Contraindicated	No interaction	No dose reduction, monitor for increased bleeding risk	No dose reduction, monitor for increased bleeding risk
Special populations (for all monitor drug levels closely)				
Hepatic impairment	Use with caution	Mild-moderate: use half dose Severe: avoid and seek expert hepatology advice	Use with caution	Severe: use with caution
Renal impairment	No dose adjustments, monitor levels closely			
Pregnancy	Avoid. Reproductive toxicity in animals and humans	Reproductive toxicity in animals, generally avoid (discuss with patient and obstetricians)		
Breastfeeding	Excreted in breast milk. Weigh benefits versus risk	No data Breast-feeding contra-indicated	Excreted into rat breast milk Breast-feeding contra-indicated	Excreted into animal breast milk Breast-feeding contra-indicated
Obesity	Limited data	Oral: no dose adjustment IV: dose adjusted to weight	Limited data	Limited data

Low body weight	Reduced dose	Reduce dose	Consider starting at lower dose	Monitor levels
Elderly	No dose adjustment Consider co-morbidities	No dose adjustment. Consider co-morbidities Visual side effects increase falls risk	No dose adjustment Consider co-morbidities	No dose adjustment Consider co-morbidities

[a]Loading doses are given in invasive disease, this is not essential for chronic disease where rapid achievement of therapeutic levels is not needed
[b]e.g. orange juice or coca cola
[c] Maximum doses stated in this clinical statement are off- label. Specialists advise from tertiary care or experienced clinicians within this area and antifungals should be consulted. Therapeutic drug monitoring is strongly recommended in these cases.
[d] Co-administration with strong enzyme inducers can influence further dose increase and therefore specialist advise is recommended in these patients. Tablet and liquid formulation of posaconazole are not interchangeable and therefore the maximum dose for liquid formulation should be in line with summary product characteristics.
[e] Currently there is insufficient data for maximum off-label doses in isavuconazole.

Supplementary Table 2: Pharmacology, and common side effects and interactions for intravenous antifungal agents active against *Aspergillus* spp.

	Liposomal Amphotericin B	**Micafungin***	**Caspofungin***
Dose	3mg/kg OD or 5mg/kg x3 / week	>40kg 150mg OD <40kg max 4mg/kg OD	70mg loading dose Maintenance dose <80kg 50mg , >80kg 70mg OD
Main adverse effects	Infusion reactions Nephrotoxicity Electrolyte disturbance (hypokalaemia, hyponatraemia, hypomagnesemia) Hepatotoxicity	Electrolyte disturbance (hypomagnesemia, hypophosphatemia, hypocalcaemia) Risk of hepatocellular tumours in rats	Electrolyte disturbance (hypomagnesemia, hypophosphatemia, hypocalcaemia)
Formulations	Liposomal 50mg powder for infusion Must be reconstituted with 5% glucose	50mg and 100mg powder for infusion	50mg and 70mg concentrate for infusion
Elimination route	Unknown	Hepatic metabolism, not CYP mediated	Spontaneous degradation
Half life	7 hours; antifungal effect lasts 12 hours	10-17 hours	Polyphasic half-life over 45 hours
Monitoring	Minimum twice weekly U+Es, magnesium, LFTs	Minimum weekly LFTs, phosphate, calcium, magnesium, U+Es	Minimum weekly liver function, calcium, magnesium, U+Es
Interactions	Caution with nephrotoxic medicines	Nil significant	Concentration decreased by CYP3A4 inducers Effective dose increased by ciclosporin
Special populations			
Hepatic impairment	Limited data	Mild-moderate; no dose adjustment Severe; caution needed	Mild; no dose reduction Moderate; Childs Pugh 7-9 reduce dose to 35mg (following 70mg loading dose) Severe; avoid
Renal impairment	No dose adjustment; use with caution	No dose adjustment	No dose adjustment
Pregnancy	Safety not established No harmful effects in animals	Avoid; reproductive toxicity in animals	Avoid; reproductive toxicity in animals

Breastfeeding	Unknown whether excreted in breast milk. Consider risks vs benefits	Excreted in animal breast milk Advise not to breastfeed	Excreted in animal breast milk Advise not to breastfeed
Obesity	Dose based on adjusted body weight Close monitoring for nephrotoxicity	If weight >115kg consider 200mg dose	Increase volume of distribution and clearance in obesity, clinical relevance unknown
Low body weight	Dose based on actual body weight Monitor renal function closely	If weight <40kg reduce to 4mg/kg	Limited information
Elderly	No dose adjustment needed Consider nephrotoxic risk	No difference in PK in elderly patients	AUC increased by 30% in elderly patients No dose adjustment needed

*Additional echinocandins therapies are likely to be available in the future (eg rezafungin)