AZOLE ANTIFUNGALS DRUG INTERACTIONS TABLE V2.1

This information on drug interactions with antimicrobials is intended for use as a guide and not as a complete reference source. Further information is available in the SmPCs of the individual medicines (section 4.5) available at www.HPRA.ie, the BNF Appendix 1 and Stockley's Drug Interactions. Please be aware that new evidence may emerge that may overtake some of these recommendations.

It is important to note that azole antifungals have many drug interactions due to CYP enzyme inhibition and effects on QT interval prolongation. The list provided is not exhaustive. Check for interactions against patient's medication before prescribing.

Antimicrobial	Interacting Drug	Comment
Azole Antifungals **Voriconazole & Posaconazole & Itraconazole**	See comments: extensive range of significant drug interactions	Extensive range of contraindications, precautions, warnings and interactions. Refer to SmPC for details.
Ketoconazole (NOTE: Ketoconazole oral tablets are no longer recommended in routine practice)		Benefit of oral ketoconazole does not outweigh risk of liver injury in fungal infections. European Medicines Agency recommends suspension of marketing authorisations for oral ketoconazole (for treatment of fungal infections). Topical ketoconazole formulations have very low systemic absorption and may continue to be used as currently approved.
Fluconazole **Miconazole oral gel** *(continued on the next two pages)*	**Statins**	*Rosuvastatin*: no clinically relevant interaction. *Pravastatin*: no clinically relevant interaction. *Atorvastatin*: use lowest possible statin dose. *Simvastatin*: may increase levels leading to rhabdomyolysis. Consider holding statin for duration of treatment or ask patient to report any unexplained muscle pain or weakness

AZOLE ANTIFUNGALS DRUG INTERACTIONS TABLE V2.1

	Interacting Drug	Comment
Fluconazole **Miconazole oral gel** *(continued from previous page, and on the following page)*	**DOACs: dabigatran, rivaroxaban, apixaban, edoxaban**	Fluconazole is predicted to increase the exposure to dabigatran. Monitor for signs of bleeding or anaemia, and discontinue dabigatran if severe bleeding occurs. Other DOACs: consult individual product literature.
	Warfarin	Increased anticoagulant effect of warfarin, increased risk of bleeding. Monitor INR closely. Co-administration of miconazole oral gel with warfarin is contraindicated except when oral miconazole gel is specifically prescribed and used under medical supervision with close monitoring of INR. Miconazole oral gel should not be dispensed over the counter to a patient on warfarin.
	Drugs that prolong QT interval* ***** *Non-drug risk factors for prolonged QT interval: Family history, Increasing age, female sex, electrolyte abnormalities (hypokalaemia, hypocalcaemia, hypomagnesaemia), cardiac ischaemia, cardiomyopathies, hypothyroidism and hypoglycaemia*	Contraindicated with erythromycin. Consult product literature for advice on concurrent drugs that prolong the QT interval E.g. antipsychotic medication including atypical antipsychotics, amiodarone & other anti-arrhythmics, some antidepressants (tricyclic antidepressants and SSRIs and MAOIs), alfuzosin, domperidone, galantamine, indapamide, lithium, methadone, quinine sulphate, tamoxifen, tizanidine. This is not a complete list, for a composite list of drugs that can prolong QT Interval please consult the relevant SmPC on HPRA website, the BNF, or www.crediblemeds.org for further information. NB: Consider OTC medication patient may be taking e.g. domperidone Citalopram/escitalopram: avoid concurrent use with fluconazole.

AZOLE ANTIFUNGALS DRUG INTERACTIONS TABLE V2.1

	Interacting Drug	Comment
Fluconazole **Miconazole oral gel** *(continued from previous two pages)*	**Phenytoin, theophylline, tacrolimus, ciclosporin, colchicine, benzodiazepines, fentanyl, NSAIDS, dutasteride, tamsulosin, zopiclone, oxycodone, buprenorphine, carbamazepine, sirolimus, calcium channel blockers, amitriptyline, ivacaftor/tezacaftor, oral hypoglycaemics/sulfonylureas**	Azole antifungals increase levels of concurrent drug, dose adjustment may be required and monitor for adverse effects (list is not exhaustive). Consult individual product literature for individual product recommendations.
	Clopidogrel	Fluconazole may reduce antiplatelet effect of clopidogrel by inhibiting the formation of active metabolite of clopidogrel.
	Colecalciferol/alfacalcidol/calcitriol	Oral miconazole (including miconazole oral gel) might decrease the efficacy of these agents. Monitor calcium and vitamin D levels.

Combined Hormonal Contraception
Extra precautions are no longer required when using combined hormonal contraception (CHC) with antibiotics (unless those antibiotics are enzyme inducers e.g. rifampicin, rifabutin). The usual additional precautions regarding vomiting, diarrhoea and non-adherence to CHC apply. Correct contraceptive practice must be adhered to.

The National Medicines Information Centre (NMIC) clinical enquiry answering service is available to prescribers in Ireland for further information about a specific drug-drug interaction(s). Contact details for the NMIC are available here.