# Antimicrobial Drug Interactions

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 BNF Appendix 1 and in the SmPCs of the individual medicines (section 4.5) available at www.HPRA.ie. Please be aware that new evidence may emerge that may overtake some of these recommendations. This table lists antimicrobials according to the frequency of use in primary care. Prescribers should be aware of the main serious drug interactions for regularly prescribed antibiotics. GPs, dentists and other community prescribers may be less familiar with some less commonly prescribed agents which may be initiated in hospital or OPAT and have the potential for serious interactions with other medicines. If a patient is prescribed an antibiotic or antifungal that you are not familiar with be alert for potential for drug interactions especially with concomitant use of statins, warfarin and non-vitamin K oral anticoagulants and antidepressants.

| Antibiotic Class | Interacting Drug | Comment |
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| **Penicillins** | **Methotrexate** | Increased risk of toxicity with methotrexate: careful monitoring for signs and symptoms of methotrexate toxicity (i.e. haematological and gastrointestinal toxicity) particularly in patients with renal impairment and the elderly. |
| **Macrolides**<br><br>e.g. Erythromycin, Clarithromycin, Azithromycin, Telithromycin | **Consult product SmPC (section 4.5) for extensive list of interacting medicines.** | Many drug interactions due to enzyme inhibition. Check for interactions against patient's medication before prescribing. |
| | **Statins** | Risk of myopathy. Avoid concomitant use (hold statin for duration of antibiotic course and for 7 days after last antibiotic dose). |
| | **Warfarin*** | Risk of bleeding. Monitor INR closely. |
| | **NOACs* - Dabigatran, Rivaroxaban, Apixaban, Edoxaban** | Monitor; increased risk of bleeding. |
| | **Drugs that prolong QT interval**** | Consider risk vs. benefit for each individual patient. Consult the currently approved SmPC for individual agents further details. (See list below for common agents) |
| | **Colchicine** | Clarithromycin, erythromycin and azithromycin possibly increase risk of colchicine toxicity—hold or reduce dose of colchicine (avoid concomitant use in hepatic or renal impairment) (BNF) |
| | **Antiepileptic drugs** | Increased plasma concentrations of carbamazepine with clarithromycin and erythromycin, phenytoin with clarithromycin and possibly valproate with erythromycin. |
| **Metronidazole** | **Warfarin*** | Enhances anticoagulant effect of warfarin. Risk of bleeding. - Monitor INR closely. |
| | **Alcohol** | A disulfiram-like reaction can occur between metronidazole and alcohol. The reaction is generally more unpleasant than serious. Warn all patients of the potential effects (flushing and tachycardia). A |

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| | | reaction can occur up to 72 hours after stopping metronidazole. |
| **Tetracyclines**<br><br>e.g. Doxycycline, Lymecycline, Minocycline | **Antacids** | Risk of reduced bioavailability and efficacy.<br>Separate the doses by 2 to 3 hours or more to avoid interaction. |
| | **Iron, Zinc, Calcium** | Risk of reduced bioavailability and efficacy.<br>Separate the doses by 2 to 3 hours or more to avoid interaction. |
| | **Warfarin*** | Risk of bleeding - monitor INR closely. |
| | **Methotrexate** | Doxycycline, tetracycline increase risk of methotrexate toxicity |
| **Trimethoprim and Co-Trimoxazole** | **Warfarin*** | May increase anticoagulant effect of warfarin with increased risk of bleeding - monitor INR closely |
| | **Methotrexate** | Risk of severe bone marrow depression and other haematological toxicities - avoid if possible |
| | **Amiodarone** | Possible increased risk of ventricular arrhythmias: avoid concomitant use of co-trimoxazole due to increased risk of arrhythmias. |
| **Quinolones**<br><br>e.g. Ciprofloxacin, Levofloxacin, Moxifloxacin | **Warfarin*** | Risk of bleeding. Monitor INR closely. |
| | **Drugs that prolong QT interval**** | Consider risk vs. benefit for each individual patient. (Moxifloxacin – contraindicated). See list below |
| | **Amiodarone** | Avoid concomitant use due to increased risk of ventricular arrhythmias |
| | **Epilepsy** | Can reduce seizure threshold. Use with caution. |
| | **Theophylline** | Ciprofloxacin can raise theophylline levels by more than 100%. Avoid combination or monitor theophylline levels on day 2 and adjust dose |
| | **Antacids** | Antacids reduce absorption of quinolones, risk of reduced bioavailability and efficacy<br>Ciprofloxacin, levofloxacin: Give at least two hours before or four hours after antibiotic dose to avoid interaction. Moxifloxacin: give at least 6 hours apart. |
| | **Iron / Calcium / phosphate binders** | Give at least two hours before or four hours after antibiotic dose to avoid interaction. |
| | **Dairy products** | Absorption of ciprofloxacin reduced by dairy products (give doses at least 2 hours apart) |

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| **Azole Anti-fungals**<br><br>e.g. Fluconazole, itraconazole Miconazole (incl. Daktarin oral gel) | **Statins** | Increased risk of myopathy. Recommended to hold the statin for duration of and 7 days after completing antifungal treatment. |
| | **NOACs: dabigatran, rivaroxaban, apixaban, edoxaban** | Not recommended - Increased plasma concentration of NOACs, increased risk of bleeding. (see individual SmPC) |
| | **Warfarin** | Increased anticoagulant effect of warfarin, increased risk of bleeding. Monitor INR closely. |
| | **Drugs that prolong QT interval**** | Consider risk vs. benefit for each individual patient. See list below. |
| (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. Topical ketoconazole formulations have very low systemic absorption and may continue to be used as currently approved.**<br>**European Medicines Agency recommends suspension of marketing authorisations for oral ketoconazole** | |
| **Voriconazole** | **Extensive range of contraindications, precautions warnings and interactions. Refer to SmPC for details** | |
| **Rifampicin** | **Warfarin** | Accelerates metabolism of warfarin resulting in reduced anticoagulant effect - monitor INR closely. |
| | **NOACs: dabigatran, rivaroxaban, apixaban, edoxaban** | Reduced plasma concentrations of NOACs resulting in reduced anticoagulant effect – avoid concomitant use |
| | **Consult product SPC for extensive list.** | Causes many drug interactions due to potent enzyme induction primarily to enzyme inhibition. Check for interactions against patient's medication before prescribing. May require dose adjustment or additional monitoring. |
| | **Oral Contraceptive Pill (OCP)** | Increased metabolism of OCP – patient should be advised to change to non-hormonal methods of birth control during rifampicin therapy and to continue using this form of contraception for two weeks after completing the course of treatment. Consult individual SmPCs for OCP as recommendations may vary regarding duration of cover required. |
| **Fusidic Acid** | **Statins** | Risk of myopathy and rhabdomyolysis. Avoid concomitant use. Hold statin for duration of antibiotic course and for 7 days after last fusidic acid dose. |

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| **Linezolid** | **Serotonergic Drugs*** ** | Caution, risk of serotonin syndrome. See list below. |
| | **Tyramine-rich foods** | Note: Linezolid is a reversible, non-selective monoamine oxidase inhibitor (MAOI) and patients should avoid large amounts of tyramine-rich foods |
| | **Other MAOIs** | Not to be given with another MAOI or within 2 weeks of stopping another MAOI (e.g. moclobemide, selegiline) |
| | **Rifampicin** | Possible therapeutic failure, rifampicin reduces plasma concentration of linezolid |
| **Carbapenems** e.g. Meropenem | **Sodium Valproate** | Contraindicated – Carbapenems reduce plasma concentration of sodium valproate: potential for inadequate seizure control. |
| **Daptomycin** | **Statins** | Risk of myopathy. Hold statin for duration of and 7 days after last dose of daptomycin. |

*** Warfarin and NOACs:** Penicillins and cephalosporins are preferred alternatives when patients are on anticoagulants. Documented reports of bleeding incidents with these antibiotics are rare even though a theoretical risk exists. Monitor INR during and after antimicrobial treatment.

**** Drugs that prolong QT interval:** Imidazoles, tricyclic antidepressants, atypical antipsychotics, amiodarone & other anti-arrhythmics, some antidepressants (citalopram, escitalopram, fluoxetine, mirtazapine, paroxetine, sertraline, trazodone, venlafaxine) alfuzosin, chlorpromazine & domperidone, galantamine, haloperidol, indapamide, lithium, methadone, quinine sulphate, tamoxifen, tizanidine, co-trimoxazole. *This is not a complete list, for a composite list of drugs that can prolong QT Interval visit [www.crediblemeds.org](http://www.crediblemeds.org).*

**Non-drug risk factors for prolonged QT interval:** Family history, electrolyte abnormalities (hypokalaemia, hypocalcaemia, hypomagnesaemia), cardiac ischaemia, cardiomyopathies, hypothyroidism and hypoglycaemia

***** Serotonergic Drugs:** Triptans (e.g. sumatriptan); antidepressants; antipsychotics; anticonvulsants; antiparkinsonian agents; analgesics (e.g., fentanyl, pethidine, tramadol); cough and cold medication containing dextromethorphan; herbal products (St. John's wort)
*This is not a complete list; please consult with product SPCs for further information.*

**Combined Hormonal Contraception**
Guidance from the UK Faculty of Sexual & Reproductive Healthcare no longer advises that extra precautions are required when using combined hormonal contraception (CHC) with antibiotics. (Unless those antibiotics are enzyme inducers e.g. rifampicin, rifabutin, isoniazid). The usual additional precautions regarding vomiting, diarrhea and non-adherence to CHC apply. Correct contraceptive practice must be adhered to.

**References: BNF June 2016, SmPCs for individual antimicrobials, Stockley's Drug Interactions, UK Faculty of Sexual and Reproductive Healthcare, www.crediblemeds.org**
**Adapted from Antimicrobial Interactions table developed by Triona O'Riordan, Senior Pharmacist, Mallow General Hospital.**