Antibiotic Class	Interacting Drug	Comment
Penicillins **e.g.** • **Amoxicillin** • **Co amoxiclav** • **Flucloxacillin** • **Phenoxymethylpenicillin**	**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.
	Warfarin	Penicillins and cephalosporins are preferred alternatives when patients are on warfarin. Documented reports of bleeding incidents with these antibiotics are rare even though a theoretical risk exists. Monitor INR during and after antimicrobial treatment and adjust warfarin dose as necessary.

Antibiotic Class	Interacting Drug	Comment
Cephalosporins **e.g.** • **Cefaclor** • **Cefixime** • **Cefuroxime** • **Cephalexin** • **Cefazolin*** • **Ceftriaxone***	**Zinc**	With cephalexin: risk of reduced bioavailability and efficacy. Separate the doses by 3 hours or more to avoid interaction.
	Warfarin	Penicillins and cephalosporins are preferred alternatives when patients are on warfarin. Documented reports of bleeding incidents with these antibiotics are rare even though a theoretical risk exists. Monitor INR during and after antimicrobial treatment and adjust warfarin dose as necessary.

Please note there are 14 potential interacting drugs listed for macrolides so please scroll to end of section

Antibiotic Class	Interacting Drug	Comment
Macrolides , e.g. • **Azithromycin** • **Clarithromycin** • **Erythromycin** **(continued on next page)**	Many drug interactions due to enzyme inhibition (CYP3A4). Check for interactions against patient's medication before prescribing. Consult product SmPC (section 4.5) for extensive list of interacting medicines.	
	Statins	Risk of myopathy with rare reports of rhabdomyolysis. *Simvastatin*: erythromycin & clarithromycin are contraindicated. If treatment with erythromycin & clarithromycin cannot be avoided suspend simvastatin for duration of antibiotic course and for 7 days after last antibiotic dose. Use of a statin that is not dependent on CYP3A metabolism (e.g. fluvastatin) can be considered. *Atorvastatin*: if co-administration of clarithromycin is necessary use lower atorvastatin doses and in any patient on >20mg clinical monitoring is recommended. Erythromycin: lower maximum dose and clinical monitoring recommended. Practical advice: if on doses >20mg reduce to 20mg for duration of macrolide treatment
	Warfarin	*Clarithromycin*: Risk of serious haemorrhage and significant elevations in INR and PT. Alternative antimicrobial advised. *Erythromycin & azithromycin*: Risk of bleeding. INR should be checked within the first 3 days of starting, during therapy and after discontinuation with warfarin dosage adjusted accordingly.
	DOACs - Dabigatran, Rivaroxaban, Apixaban, Edoxaban	*Dabigatran*: increased levels of dabigatran, monitor for adverse effects (such as bleeding), adjusting dose of dabigatran if appropriate. Discontinue dabigatran if severe bleeding occurs. *Rivaroxaban*: may increase levels, not clinically significant, no action needed *Apixaban*: *clarithromycin:* alternative antimicrobial advised. *Erythromycin & azithromycin*: monitor for signs of bleeding. *Edoxaban*: reduce dose to 30mg for DVT & PE, no dose change for NVAF, monitor for signs of bleeding.

Antibiotic Class	Interacting Drug	Comment
Macrolides , e.g. • **Azithromycin** • **Clarithromycin** • **Erythromycin** **(continued from previous and page)**	**Drugs that prolong QT interval** *	Macrolides are strongly advised against in patients on medications that prolong the QT interval: Consider alternatives or seek advice: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
	Colchicine	Clarithromycin, erythromycin and azithromycin possibly increase risk of colchicine toxicity. Concomitant administration of clarithromycin and colchicine is contraindicated
	Antiepileptic drugs	Increased plasma concentrations of carbamazepine with clarithromycin and erythromycin, phenytoin with clarithromycin and possibly valproate with erythromycin.
	Immunosuppressants	Ciclosporin, tacrolimus, sirolimus: *erythromycin & clarithromycin*: alternative antimicrobial advised, *azithromycin*: caution
	Oral hypoglycemic agents/Insulin	Concomitant use can result in hypoglycaemia. Careful monitoring of glucose is recommended.
	Benzodiazepines	Increase in exposure to alprazolam, triazolam and midazolam expected with clarithromycin and erythromycin. Monitor for increase in benzodiazepine adverse effects (e.g. sedation). Caution with driving / skilled tasks.
	Digoxin	Increase in exposure to digoxin. Monitor digoxin levels and signs of digoxin toxicity (e.g. bradycardia)
	Anti-rejection medicines: Ciclosporin, Tacrolimus, Sirolimus	Increased plasma levels of anti-rejection medicines expected. Sirolimus contra-indicated with clarithromycin. See individual SPCs for recommendations.
	Ticagrelor	Contraindicated with clarithromycin due to marked increase in Ticagrelor exposure, caution use with azithromycin.
	Ranolazine	Contraindicated with clarithromycin. Careful dose titration of ranolazine with erythromycin as increase in exposure to ranolazine likely.
	Lercanidipine	Contraindicated with clarithromycin and erythromycin, markedly increased exposure to lercanidipine.

*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.

Antibiotic Class	Interacting Drug	Comment
Tetracyclines **e.g.** • **Doxycycline** • **Lymecycline** • **Minocycline**	**Antacids**	Risk of reduced bioavailability and efficacy. Separate the doses by 2 to 3 hours or more to avoid interaction.
	Iron, Zinc, Calcium, Magnesium	Risk of reduced bioavailability and efficacy. 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
	Systemic retinoids. e.g. isotretinoin	Concomitant use of retinoids and tetracyclines should be avoided because of a risk of causing benign intracranial hypertension.
	Antiepileptics	Doxycycline levels may be reduced. Monitor for efficacy and consider increase in doxycycline dose.
	Rifampicin	Doxycycline levels may be reduced. Monitor for efficacy and consider increase in doxycycline dose.

Antibiotic Class	Interacting Drug	Comment
Metronidazole	**Warfarin**	Enhances anticoagulant effect of warfarin. Risk of bleeding. The INR should be checked frequently and warfarin dosage adjusted accordingly, particularly following initiation or discontinuation of metronidazole
	Alcohol	A disulfiram-like reaction can occur between metronidazole and alcohol. The reaction is generally more unpleasant than serious. Patients should be advised not to take alcohol, (or drugs containing alcohol) during metronidazole therapy and for at least 48 hours afterwards because of a disulfiram-like (antabuse effect) reaction (flushing, vomiting, tachycardia).

Antibiotic Class	Interacting Drug	Comment
Rifampicin	**Warfarin**	Accelerates metabolism of warfarin resulting in reduced anticoagulant effect - monitor INR closely, dose increases may be required and effect can persist for 2-5 weeks after stopping rifampicin
	DOACs: dabigatran, rivaroxaban, apixaban, edoxaban	Reduced plasma concentrations of DOACs resulting in reduced anticoagulant effect – avoid concomitant use. Consider either an alternative antimicrobial or an alternative anticoagulant,
	Consult product SmPC 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)	**Short-term treatment**: Women on treatment with enzyme-inducing drugs should temporarily use a barrier method or another method of contraception in addition to the COC. The barrier method must be used during the whole time of the concomitant drug therapy and for 28 days after its discontinuation. **Long-term treatment:** In women on long-term treatment with hepatic enzyme-inducing active substances, another reliable, non-hormonal, method of contraception is recommended.

Please note there are 12 potential interacting drugs listed for Quinolones so please scroll to end of section

Antibiotic Class	Interacting Drug	Comment
Quinolones **e.g.** • **Ciprofloxacin** • **Levofloxacin** • **Moxifloxacin** • **Ofloxacin** **(continued on next page)**	**Warfarin**	Risk of bleeding. Monitor INR closely and adjust warfarin dose as necessary.
	Drugs that prolong QT interval*	Ciprofloxacin & levofloxacin should be used with caution in patients receiving medicines known to prolong QT interval (e.g. Class IA and III anti-arrhythmics e.g. amiodarone, tricyclic antidepressants, macrolides, antipsychotics) and in patients with known risk factors for prolongation of the QT interval.** Moxifloxacin is contraindicated with 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, macrolides, 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
	Methotrexate	Co administration of methotrexate with ciprofloxacin may increase the plasma concentrations of methotrexate leading to increased risk of methotrexate-associated toxic reactions. Concomitant use is not recommended.
	Aminophylline, theophylline, NSAIDs	Increased risk of convulsions
	Epilepsy	Can reduce seizure threshold. Use with caution.
	Ciclosporin	Increased risk of nephrotoxicity
	Theophylline and other drugs metabolised by CYP1A2 e.g. clozapine, olanzapine, ropinirole, duloxetine	Ciprofloxacin inhibits CYP1A2 and may cause increased serum concentration of substances metabolised by this enzyme (e.g. theophylline, clozapine, olanzapine, ropinirole, tizanidine, duloxetine, agomelatine). Ciprofloxacin can raise theophylline levels by more than 100%. This can lead to theophylline-induced side effects that may rarely be life threatening or fatal. Avoid combination or if it is necessary to use both medicines patients should be closely monitored; monitor theophylline levels on day 2 and adjust dose. Monitor for clozapine adverse effects (e.g. agitation, dizziness, sedation, hypersalivation), adjust the dose as necessary, to one third of usual clozapine dose.

*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.

Antibiotic Class	Interacting Drug	Comment
Quinolones **e.g.** • **Ciprofloxacin** • **Levofloxacin** • **Moxifloxacin** • **Ofloxacin**	**Tizanidine**	Tizanidine is metabolised by CYP1A2 and is contraindicated with ciprofloxacin. Increased serum tizanidine concentration is associated with a potentiated hypotensive and sedative effect.
	Phenytoin	Administration of ciprofloxacin and phenytoin may lead to reduced serum phenytoin levels. Monitoring of phenytoin levels is recommended when initiating or discontinuing ciprofloxacin. Adjustment of phenytoin dose may be required. Quinolones can reduce seizure threshold. Use with caution in patients with epilepsy.
(continued from previous page)	**Antacids**	Antacids reduce absorption of quinolones, risk of reduced bioavailability and efficacy *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, magnesium, aluminium, zinc	Give at least two hours before or four hours after antibiotic dose to avoid interaction.
	Dairy products and fortified drinks	Absorption reduced by dairy products (give doses at least 2 hours apart)

Antibiotic Class	Comment
Voriconazole & Posaconazole & Itraconazole	Extensive range of contraindications, precautions, warnings and interactions. Refer to SmPC for details
(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. European Medicines Agency recommends suspension of marketing authorisations for oral ketoconazole

Antibiotic Class	Interacting Drug	Comment
Azole Antifungals e.g. • **Fluconazole** • **Miconazole oral gel**	Statins	*Rosuvastatin*: no clinically relevant interaction *Pravastatin*: no clinically relevant interaction *Atorvastatin*: used 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
	DOACs: dabigatran, rivaroxaban, apixaban, edoxaban	An increased risk of major bleeding in patients co-administered fluconazole with DOACs.
	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*	Contraindicated with erythromycin Caution is advised with 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
	Phenytoin, theophylline, tacrolimus, ciclosporin, benzodiazepines, fentanyl, celecoxib, methadone, carbamazepine, sirolimus, calcium channel blockers, amitriptyline, ivacaftor/tezacaftor	Increased levels of drug, dose adjustment may be required
	Clopidogrel	Fluconazole may reduce antiplatelet effect of clopidogrel by inhibiting the formation of active metabolite of clopidogrel.

*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.

Antibiotic Class	Interacting Drug	Comment
Trimethoprim and Co-Trimoxazole	**Warfarin**	May increase anticoagulant effect of warfarin with increased risk of bleeding - monitor INR closely
	Methotrexate and other bone marrow depressants e.g. azathioprine, mercaptopurine.	Alternative antibiotic recommended. Several cases of severe bone marrow depression (several fatal) have resulted from the concurrent use of low-dose methotrexate and co-trimoxazole or trimethoprim. With other bone marrow depressants, close monitoring of haematological toxicity is recommended
	Tacrolimus, Ciclosporin	Alternative antibiotic recommended. May cause additive nephrotoxicity. If combination required more frequent drug levels of the immunosuppressant may be required.
	Amiodarone	Possible increased risk of ventricular arrhythmias: avoid concomitant use of co-trimoxazole due to increased risk of arrhythmias.
	Potassium sparing diuretics e.g. eplenerone and thiazide diuretics, angiotensin 2 antagonsists e.g. valsartan and ACE inhibitors e.g. perindopril	Trimethoprim in combination with these agents or potassium salts may increase the risk of hyperkalaemia or hyponatraemia. Patients should be monitored closely particularly if receiving high-dose or long-term trimethoprim treatment.
	Dapsone	Increased risk of methaemoglobinaemia with dapsone and trimethoprim co-administration.
	Clozapine	Contraindicated, risk of neutropenia. If concurrent use necessary, increase monitoring FBC, including absolute neutrophil count.
	Digoxin	Increase in exposure to digoxin. Monitor digoxin levels and signs of digoxin toxicity (e.g. bradycardia).
	Phenytoin	Co-trimoxazole prolongs the half-life of phenytoin. Close monitoring of the patients conditions and serum phenytoin levels is advisable.

Antibiotic Class	Interacting Drug	Comment
Oral Fusidic Acid	**Statins**	Risk of myopathy and rhabdomyolysis (including fatalities). Avoid concomitant use. Hold statin for duration of antibiotic course and for 7 days after last fusidic acid dose.

Antibiotic Class	Interacting Drug	Comment
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)
	Agents that increase BP	Monitor BP closely with agents that increase BP e.g. adrenaline, noradrenaline, pseudoephedrine, dopamine, droxodopa, methylphenidate
	Rifampicin	Possible therapeutic failure, rifampicin reduces plasma concentration of linezolid

****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 SmPCs for further information.

Symptoms of Serotonin Syndrome

Alteration of mental status: agitation, confusion, delirium, hallucinations, drowsiness, coma

Neuromuscular hyperactivity: profound shivering, tremor, teeth grinding, myoclonus, ocular clonus, spontaneous clonus, hyperreflexia
Autonomic instability dilated pupils, diarrhoea, profuse sweating, flushing, tachycardia, hyper/hypotension

In severe cases, hyperthermia, rhabdomyolysis, renal failure, and disseminated intravascular coagulopathy may develop

Antibiotic Class	Interacting Drug	Comment
Carbapenems* e.g. Meropenem, ertapenem**	**Sodium Valproate**	Contraindicated – Carbapenems reduce plasma concentration of sodium valproate: potential for inadequate seizure control.

Antibiotic Class	Interacting Drug	Comment
Daptomycin*	**Statins**	Risk of myopathy. Hold statin for duration of and 7 days after last dose of daptomycin.
	Ciclosporin	The manufacturer suggests temporarily withdrawing ciclosporin. If this is not possible creatine kinase should be monitored more frequently (i.e. more than once weekly).

Antibiotic Class	Interacting Drug	Comment
Tigecycline*	**Warfarin**	Monitor INR with concurrent use and adjust warfarin dose accordingly

Antibiotic Class	Interacting Drug	Comment
Caspofungin*	**Rifampicin Phenytoin Carbamazepine Dexamethasone**	Reduced caspofungin plasma concentration. Recommend daily dose of 70mg for adults, regardless of weight.
	Tacrolimus	Increase in tacrolimus plasma concentration expected. Monitor tacrolimus levels and adjust dose as necessary.

*** Patient may be on via OPAT outpatient parenteral antimicrobial therapy

Antimicrobial Class	Interacting Drug	Comment
Antiviral Neuraminidase inhibitors e.g. Oseltamivir Zanamivir	Live vaccines (e.g. Fluenz Tetra®)	*Fluenz Tetra*® should not be administered until 48 hours after stopping oseltamivir/zanamivir as there is potential for the anti-viral agents to reduce the effectiveness of Fluenz Tetra®. Oseltamivir/zanamivir should not be given within two weeks after receiving Fluenz Tetra® vaccination as they may affect the response of the vaccine. If oseltamivir/zanamivir and Fluenz Tetra® are administered concomitantly, revaccination should be considered based on clinical judgement.
	Leflunomide	*Oseltamivir:* may increase levels of oseltamivir, monitor for adverse effects and adjust dose of oseltamivir if required.
	Tolvaptan	*Oseltamivir:* may increase levels of oseltamivir, monitor for adverse effects and adjust dose of oseltamivir if required.
	Warfarin	*Oseltamivir:* Isolated cases of raised INRs have been reported.

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, isoniazid). The usual additional precautions regarding vomiting, diarrhoea and non-adherence to CHC apply. Correct contraceptive practice must be adhered to.