TABLE 170-4 SIGNIFICANT ANTIBACTERIAL DRUG INTERACTIONS

Antibacterial(s)	Interacting Agent(s)	Potential Effect and Management
Nafcillin	Warfarin, cyclosporine, tacrolimus	Decreased levels of warfarin, cyclosporine via CYP3A4 induction. Monitor levels of affected drug closely if drugs are given concomitantly.
Ceftriaxone	Calcium-containing IV solutions	Concomitant use is contraindicated in neonates (<28 days); the combination can lead to precipitation of ceftriaxone-calcium particulate.
		Ceftriaxone and calcium-containing solutions can be given to infants >28 days of age provided they are given sequentially and the lines are thoroughly flushed between infusions.
Carbapenems	Valproic acid	Decreased levels of valproic acid. Monitor valproic acid levels closely if drugs are given concomitantly.
Linezolid, tedizolid	Serotonergic and adrenergic agents (e.g., SSRIs, vasopressors)	Increased levels of serotonergic and adrenergic agents. Monitor for serotonin syndrome. Tedizolid may have less potential than linezolid to cause this drug interaction.
Quinupristin dalfopristin	Substrates of cytochrome CYP3A4 (e.g., warfarin, ritonavir, cyclosporine, diazepam, verapamil)	Can result in increased levels of interacting drug. Erythromycin and clarithromycin are more potent CYP3A4 inhibitors than azithromycin. Avoid concomitant administration if possible.
Fluoroquinolones	Theophylline[a]	Can result in theophylline toxicity
	Sucralfate; antacids containing aluminum, calcium, or magnesium; ferrous sulfate and zinc-containing multivitamins	Can result in subtherapeutic fluoroquinolone levels. Administer fluoroquinolone 2 h before or 6 h after interacting drug.
	Tizanidine[a]	Can result in increased levels of tizanidine and hypotensive, sedative effects. Monitor for side effects if drugs are given concomitantly.
Rifampin	Substrates of cytochrome CYP3A4 (e.g., warfarin, ritonavir, cyclosporine, diazepam, verapamil, protease inhibitors, voriconazole)	Can result in decreased levels of interacting drug. Avoid concomitant use if possible. If giving drugs concomitantly, monitor drug levels if possible.
	Substrates of cytochrome CYP2C19 (e.g., omeprazole, lansoprazole)	
	Substrates of cytochrome CYP2C9 (e.g., warfarin, tolbutamide)	
	Substrates of cytochrome CYP2C8 (e.g., repaglinide, rosiglitazone)	
	Substrates of cytochrome CYP2B6 (e.g., efavirenz)	
	Hormone therapy (e.g., norethindrone)	Can result in decreased levels of hormone. If oral contraceptive and rifampin are given concomitantly, use alternative form of birth control.
Tetracyclines	Antacids or drugs containing calcium, magnesium, iron, or aluminum	Can result in decreased absorption of tetracyclines. Administer tetracycline 2 h before or 6 h after interacting drug.
Macrolides[b]	Substrates of cytochrome CYP3A4 (e.g., warfarin, ritonavir, cyclosporine, diazepam, verapamil)	Avoid concomitant administration if possible.
	QTc-prolonging agents (e.g., fluoroquinolones, sotalol)	Increased risk of cardiotoxicity and arrhythmias. Monitor QTc.
	Protease inhibitors (e.g., ritonavir)	Can result in increased levels of both macrolides and protease inhibitors. Avoid concomitant use if possible.
	Cimetidine	Cimetidine can increase levels of macrolides.
Metronidazole	Ethanol	Can result in disulfiram-like reaction. Ethanol may be present in some formulations of oral drug suspensions (e.g., ritonavir).
	Warfarin	Can increase warfarin levels. Monitor INR closely if drugs are given concomitantly.
TMP-SMX	Warfarin	Increased effect of warfarin. Monitor levels closely if drugs are given concomitantly.
	Phenytoin	Increased levels of phenytoin. Monitor levels closely if drugs are given concomitantly.
	Methotrexate	Increased levels of methotrexate. Monitor levels closely if drugs are given concomitantly.
Oritavancin	Substrates of cytochrome CYP3A4 (e.g., cyclosporine, warfarin) and CYP2D6 (e.g., aripiprazole)	Can result in decreased levels of interacting drug. Avoid concomitant use if possible. If giving drugs concomitantly, monitor drug levels if possible.
	Substrates of cytochrome CYP2C19 (e.g., omeprazole) and CYP2C9 (e.g., warfarin)	Can result in increased levels of interacting drug. Avoid concomitant use if possible. If giving drugs concomitantly, monitor drug levels if possible.

[a]Drug reaction described with ciprofloxacin only. [b]Clarithromycin and erythromycin are potent CYP3A4 inhibitors; the probability of a drug interaction with azithromycin is lower.

Abbreviations: INR, international normalized ratio; SSRI, selective serotonin-reuptake inhibitor; TMP-SMX, trimethoprim-sulfamethoxazole.

but typically inhibit the *S. aureus* class A β-lactamase, β-lactamases of *H. influenzae* and *Bacteroides* species, and a number of plasmid-encoded β-lactamases. These combination agents are typically used when broader-spectrum coverage is needed—e.g., in pneumonia and intraabdominal infections. Piperacillin-tazobactam is a useful agent for broad coverage in febrile neutropenic patients. The combination agents, however, are not effective against organisms that produce AmpC β-lactamases or carbapenemases.

Cephalosporins The cephalosporin drug class encompasses five generations determined by spectrum of antibacterial activity. The first generation (cefazolin, cefadroxil, cephalexin) largely has activity