TABLE 16 Pharmacokinetic Drug-Drug Interactions With Antihypertensive Medications

Blood Pressure Drug	Potential Interacting Drug	Clinical Effect
Absorption		
Thiazide-type diuretics	Cholestyramine	Decreased absorption leading to reduced BP lowering
Amlodipine, furosemide, metoprolol, carvedilol, bisoprolol, nebivolol, telmisartan	Potassium binder (patiromer)	Decreased absorption of antihypertensives leading to reduced BP-lowering effects. To mitigate this, administer the antihypertensives at least 3 h before or after taking the potassium binder
Furosemide	Potassium binder (sodium zirconium cyclosilicate)	Increased absorption of furosemide due to increased gastric pH leading to increased clinical effects (eg, diuresis or risk of hypokalemia); effect diminished with separation of administration by 2 h
Methyldopa	Iron salts	Decreased absorption of methyldopa leading to reduced BP lowering
Metabolism		
Bisoprolol, carvedilol, metoprolol	CYP2D6 inhibitors (eg, amiodarone, cimetidine, diphenhydramine, fluoxetine, paroxetine, terbinafine)	Increased BB concentration leading to enhanced clinical effects (eg, hypotension and bradycardia)
Diltiazem, verapamil	CYP3A4 inhibitors (eg, clarithromycin, erythromycin itraconazole, ketoconazole)	Increased nondihydropyridine concentration leading to enhanced clinical effects (eg, hypotension and bradycardia)
Diltiazem, verapamil	CYP3A4 inducers (eg, carbamazepine, phenobarbital, phenytoin, St. John's Wort, rifampin)	Decreased nondihydropyridine CCB concentration leading to reduced clinical effects (eg, minimization of blood pressure and pulse lowering)
CYP3A4 inhibition via amlodipine, verapamil, or diltiazem or other CYP3A4 inhibitors	Tacrolimus, cyclosporine	Increased calcineurin inhibitor concentration leading to increased risk for side effects (eg, renal impairment)
	Dabigatran, rivaroxaban	Increased concentration leading to increased risk for bleeding
	Atorvastatin, simvastatin	Increased statin concentration leading to increased risk for side effects (eg, myopathy)
	Colchicine	Increased colchicine concentration leading to increased risk for adverse effects (eg, neuromuscular toxicity)
	Eplerenone	Increased risk of hypotension and hyperkalemia Using a lower dose of eplerenone when combined with diltiazem could be considered a productive interaction, as the inhibition of eplerenone's metabolism might allow for lower doses to be effective, reducing the risk of adverse effects while maintaining efficacy
Elimination		
Lithium	Thiazide-type diuretics, RAS blockers	Reduced lithium clearance leading to increased lithium toxicity risk
P-glycoprotein (P-gp)		
Verapamil via P-gp inhibition	Dabigatran	Reduced P-gp efflux of dabigatran leading to increased dabigatran levels, which results in a higher risk of bleeding
Verapamil and carvedilol via P-gp inhibition	Digoxin	Reduced P-gp efflux of digoxin leading to increased digoxin levels, resulting in a higher risk of digoxin toxicity

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BB indicates beta blocker; BP, blood pressure; CCB, calcium channel blocker; h, hour; and P-gp, P-glycoprotein.

inhibitors of CYP3A4 and can alter the metabolism of other medications processed through this pathway. Table 16 summarizes other key clinical pharmacokinetic drug-drug interactions. Examples of beneficial pharmacodynamic interactions include the combination of an RAS inhibitor with a thiazide-type diuretic to minimize diuretic-induced hypokalemia, or a dihydropyridine CCB with an RAS inhibitor to reduce the incidence or severity of lower extremity edema. Conversely, combining drugs with overlapping mechanisms, like ACEi and ARB or direct renin inhibitors, leads to an increased risk of hyperkalemia, an adverse pharmacodynamic interaction. Table 17 lists other key pharmacodynamic drug-drug interactions affecting antihypertensive medications.