Xarelto (rivaroxaban)

- Absorption is mediated by P-gp and metabolism by CYP3A4
- Medications that interfere with both P-gp and CYP3A4 are likely to cause more significant interactions than medications that interfere with P-gp or CYP3A4 alone

Drug Class	Examples	Effect	Label Recommendations	Suggested Action/Notes
Combined P-gp inhibitor & strong CYP3A4 inhibitor	Itraconazole, ketoconazole, HIV protease inhibitors, conivaptan, clarithromycin*	Significant ↑ increase in rivaroxaban exposure	Avoid concomitant use *No precautions are necessary with clarithromycin per package insert	Avoid concomitant use Risk higher in pts with renal impairment
Combined P-gp inhibitor and moderate CYP3A4 inhibitor or strong CYP3A4 inhibitor alone	Amiodarone, azithromycin, cyclosporine, diltiazem, dronedarone, erythromycin, fluconazole, verapamil, nicardipine, quinidine, ranolazine, tamoxifen, ticagrelor, verapamil, voriconazole	**Normal renal function**: moderate increase ↑ in rivaroxaban exposure **Renal impairment**: significant increase ↑ in rivaroxaban exposure	Do not use in patients with CrCl 15-79 mL/min who are receiving combined P-gp and moderate CYP3A4 inhibitors *unless* benefit > risk	Use with caution in pts with normal renal function Avoid use in patients with renal impairment
Combined P-gp inducer & strong CYP3A4 inducer	Carbamazepine, dexamethasone, phenytoin, fosphenytoin, rifampin, St. John's Wort, phenobarbital, primidone	Significant decrease in rivaroxaban exposure	Avoid concomitant use	Avoid concomitant use Effect may persist for several weeks following d/c of strong inducers of P-gp and/or CYP3A4
P-gp inducer	Tipranavir	May decrease rivaroxaban exposure	Not addressed	Consider alternative
Strong CYP3A4 inducer	Barbiturates, efavirenz, nafcillin, bosentan			

Eliquis (apixaban)

- CYP3A4 major substrate & P-gp substrate

Drug Class	Examples	Effect	Label Recommendations	Suggested action/Notes
Combined P-gp inhibitor and strong CYP3A4 inhibitor	Ketoconazole, itraconazole, ritonavir	Significant increase in apixaban exposure	Decrease by 50 % if receiving 5 mg or 10 mg BID Avoid coadministration if receiving 2.5 mg BID	Although clarithromycin is a combined P-gp and strong CYP3A4 inhibitor, no dose adjustment is necessary
Combined P-gp inducer and strong CYP3A4 inducer	Rifampin, carbamazepine, phenytoin, St. John's wort, primidone	Significant decrease in apixaban exposure	Avoid concomitant use	
Strong CYP3A4 inhibitor	Fluconazole, protease inhibitors, voriconazole	Increase exposure of apixaban	Not addressed	Monitor for signs of increased exposure

Pradaxa (dabigatran)

- P-glycoprotein (P-gp) substrate

Drug Class	Examples	Effect	Label Recommendations	Suggested Action	Notes
P-gp inhibitor	Quinidine, verapamil, clarithromycin, ketoconazole, amiodarone, dronedarone, itraconazole	Increased exposure of dabigatran	**Deep venous thrombosis/pulmonary embolism:** CrCl <50 mL/minute: Avoid concomitant use **Nonvalvular atrial fibrillation:** CrCl 30-50 mL/min: 75 mg BID with *dronedarone or ketoconazole* CrCl < 30 mL/min: Avoid concomitant use	Adjust based on indication and CrCl	Consider dosing dabigatran 2 hours prior to verapamil, quinidine, and dronedarone Ketoconazole ↑ dabigatran exposure by 150%. The use of verapamil, amiodarone, quinidine, clarithromycin, and ticagrelor does not require a dose adjustment.
P-gp inducer	Rifampin, St. John's Wort, phenytoin, fosphenytoin, carbamazepine, primidone	Decreased exposure of dabigatran	Avoid concomitant use	Avoid concomitant use	Rifampin decreases dabigatran exposure by 67%
Antacids	Pantoprazole, calcium carbonate	Decreased bioavailability of dabigatran	Not addressed	May consider avoidance of acid suppression therapy	Decreased dabigatran solubility at pH > 4