DRUG	EFFECT ON INR	MECHANISM	ANTICIPATED ONSET	ANTICIPATED OFFSET	SUGGESTED MANAGEMENT
Amiodarone	Mod-Severe ↑	Inhibition of warfarin metabolism (2C9); inducing hypo-or hyperthyroidism	3-7 days	~90 days (variable) $t_{1/2}$ = 26-107 days	Consider 10-25% warfarin dose reduction within first week of starting amiodarone, with anticpated eventual reductions up to 60%; If loading dose amiodarone used, interaction will occur sooner.
Azithromycin	Moderate ↑	Possible decrease in warfarin metabolism	3-7 days	NR $t_{1/2}$ = 68 hrs	Monitor INR; Inconsistent effect; No empiric reduction
Carbamazepine	Mod-Severe ↓	Increase in warfarin metabolism (2C9)	10-35 days	14-40 days (delayed) $t_{1/2}$ = 68 hrs	Consider increase in warfarin dose 50-100% when starting carbamezapine and decreasing warfarin dose by 50% when stopping
Ciprofloxacin	Moderate ↑	Unknown; Possible 1A2 inhibition or decrease in Vit K producing bacteria	2-5 days	2-4 days $t_{1/2}$ = 3-6 hrs	Some experience increase in INR; some have no effect. May consider 10-15% warfarin dose reduction
Doxycycline	Moderate ↑	Unknown; Possible 3A4 inhibition or protein binding displacement	2-5 days	NR $t_{1/2}$ = 15-24 hrs	Monitor INR; No empiric reduction
Fluconazole	Moderate ↑	Inhibition of warfarin metabolism (CYP 2C9 and 3A4)	2-3 days	7-10 days $t_{1/2}$ = 30 hrs	Consider 25-30% warfarin dose reduction with eventual reductions up to 80%; More pronounced in patients with impaired renal fuction
Levofloxacin	Moderate ↑	Unknown; Possible 1A2 inhibition or decrease in Vit K producing bacteria	3-5 days	5-10 days $t_{1/2}$ = 3-6 hrs	Some experience increase in INR; some have no effect. More common clinically significant in elderly. May consider 0-15% warfarin dose reduction
Levothyroxine	Moderate ↑	Patients with hypothyroidism have higher requirements of warfarin due to decreased catabolism of clotting factors; Correcting hypothyroidism decreases warfarin requirements	1-2 weeks	1-2 weeks $t_{1/2}$ = 6-7 days	When starting or adjusting levothyroxine dose, no empiric reduction required; Adjust warfarin gradually according to INR results
Metronidazole	Major ↑	Inhibition of warfarin metabolism (CYP 2C9)	3-5 days	~2 days $t_{1/2}$ = 8 hrs	Consider empiric 25-40% warfarin dose reduction
Phenobarbital	Moderate ↓	Induction of hepatic metabolism of warfarin	Delayed	NR $t_{1/2}$ = 1.5-4.9 days	Monitor INR; May require 30-60% increase in warfarin dose after barbiturate initiation
Phenytoin	Moderate ↑ ↓	Initially, displacement of warfarin from protein binding sites, with long term use, induction of hepatic metabolism of warfarin	Initial: 1-3 days Subsequent: 2-4 weeks	10-14 days $t_{1/2}$ = 22 hrs	No empiric dose adjustment when phenytoin is initiated; Adjust phenytoin gradually according to INR results (may ultimately require up to 50% increase in warfarin dose several weeks after phenytoin is initiated)
Prednisone	Mild ↑ ↓	Unknown	Delayed	NR $t_{1/2}$ = 2.6-3 hrs	No empiric dose adjustment when initiating prednisone/steroids; warfarin dose adjustment may be required for patients receiving large bolus or pulse dose of steroids
Rifampin	Mod-Severe ↓	Induction of hepatic metabolism of warfarin	1-3 weeks	1-5 weeks $t_{1/2}$ = 1.5-5 hrs	Consider 25-50% warfarin dose increase initially with further adjustments based on INR results; May require 2-3 x regular weekly warfarin dose
Simvastatin	Mild-Mod ↑	Competition for CYP 3A4 mediated metabolism	3-7 days	3-7 days $t_{1/2}$ = 3 hrs	Monitor INR; Inconsistent effect; No empiric reduction
Sulfamethoxazole (w/wo trimethoprim)	Severe ↑	Inhibition of warfarin metabolism (CYP 2C9) and displacement of warfarin from protein binding sites	2-5 days	2-14 days $t_{1/2}$ = 10 hrs	Consider 25-50% empiric warfarin dose reduction

Reference: Bungard TJ, et al. *CPJ/RPC* 2011; 144(1): 21-25.e9