รายการยาที่มีรายงานอันตรกิริยากับยา warfarin (Practical tool - Warfarin drug interaction)

Drug	Direction and severity of effect on INR	Mechanism	Anticipated onset	Anticipated offset (t½)†	Suggested management	Significant	ข้อมูลเพิ่มเติม
Acarbose	↑ INR Moderate	Unknown: effect may be due to increase in warfarin absorption or to drug- associated diarrhea	2–3 days	(t ½ = 2 hours) ระดับ INR กลับมาคงที่ใช้เวลา 7-14 วัน หลังหยุดยา Acarbose*	Monitor INR closely when starting or stopping acarbose	4	*Morreale AP, et al. Am J Health Syst Pharm. 1997;54(13):1551
Acetaminophen (doses >2 g/d)	↑ INR Moderate	Decrease in warfarin metabolism and/or decrease in production of clotting factors	2–5 days	(t½ = 2–4 hours) หยุดยา 2 วันแล้วกลับมาปกติ*	Monitor INR when starting or stopping higher doses of acetaminophen; minimize use of drug (e.g., <2 g/d for short courses[<1 week])	2	* Gebauer MG, et al. Pharmacotherapy. 2003 Jan;23(1):109-12.
Allopurinol	↑ INR Major	Unknown	3–5 days	NR (t½ = 1–2 hours; foractive metabolite,oxypurinol, t½ = 15–25 hours)	Reports of interaction are inconsistent; monitor INR when starting or stopping allopurinol Reassess in 1 week	4	
Amiodarone	↑ INR Moderate to severe	Inhibition of warfarin metabolism; amiodarone may also increase or reduce INR by inducing hyper- or hypo-thyroidism, respectively	3–7 days ทำให้ระดับ INR เพิ่มขึ้นอย่างช้าๆ ในช่วง 2-4 สัปดาห์แรก**	~ 90 days; may be longer if amiodarone therapy is prolonged (t½ = 26–107 days) หลังจากหยุดยา INR ลดลงอย่างช้าๆ ในช่วง 4-12 สัปดาห์หลังหยุดยา amiodarone**	Monitor INR closely (i.e., weekly) when starting or stopping amiodarone; if loading doses of amiodarone are used, interaction will occur sooner; AMS considers empiric 10%–25% warfarin dose reduction 1 week after starting amiodarone, in anticipation of eventual dose reductions of up to 60%ให้ติดตาม INR ทุก 1-2 สัปดาห์ในช่วง 12 สัปดาห์แรกที่ทานยา	1	*Lu, et al.Am J Health Syst Pharm May 15, 2008; 65(10):947-952.4.**Kurnik, Daniel MD; et al. Medicine (Baltimore). 2004 Mar;83(2):107-13.
Amprenavir	↑ INR Moderate	May inhibit warfarin metabolism (through CYP3A4 inhibition)	Delayed	Delayed (t½ = 7–10 hours)	Monitor INR more frequently when starting or stopping amprenavir; addition of ritonavir booster (CYP2C9, CYP1A2 inducer) may result in net decrease in INR; see entry for ritonavir for additional information	4	

ASA	No effect at doses < 6 g/d, ↑ risk of bleeding Major	Irreversible inhibition of platelet function	1–3 days	5–7 days (inhibitory effects of ASA on platelets last for lifetime of each platelet)	Use lowest effective dose of ASA; use enteric-coated formulation; monitor for bleeding	1	
Atazanavir	↑ INR Moderate	May inhibit warfarin metabolism (through CYP3A4 inhibition)	Delayed	Delayed ($t_{1/2}$ = ~7 hours)	Monitor INR more frequently when starting or stopping atazanavir; addition of ritonavir booster (CYP2C9, CYP1A2 inducer) mayresult in net decrease in INR; see entry for ritonavir for additional information	4	
Azathioprine and mercaptopurine	↓ INR Moderate	Possible increase in warfarin metabolism	1–3 days	NR ($t_{1/2}$ = 5 hours)	Monitor INR when azathioprine therapy is started or discontinued or dosage is adjusted; significantly more (2- to 3-fold) warfarin may be required when given concurrently with azathioprine	2	
Azithromycin	↑ INR Major	Possible decrease in warfarin metabolism; interaction is often compounded by other factors that may increase INR (e.g., fever, decreased appetite)	3–7 days	NR ($t_{1/2}$ = 68 hours)	Inconsistent effect; monitor INR closely when starting or stopping azithromycin; AMS will not empirically decrease warfarin unless patient has other factors affecting INR (e.g., fever, decreased appetite)	1	
Barbiturates (amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, primidone, secobarbital)	↓ INR Major	Induction of hepatic metabolism of warfarin	Delayed เริ่มเห็นผลภายใน 14 วันนับจากวันที่เริ่มยา phenobarbital*	NR ($t_{1/2}$ = 1.5–4.9 days) เมื่อหยุดยา phenobarbital การ metabolism ยา warfarin จะลดลงภายใน 2 สัปดาห์*	Monitor INR closely, especially when starting or stopping phenobarbital or barbiturates; according to published reports, 30%–60% wafarin dose increases may be required after barbiturate initiation	1	*MacDonald MG,Robinson DS. Clinical observations of possible barbiturate interference with anticoagulation. JAMA 1968 Apr 8;204(2):97-100.

Bismuth subsalicylate	↑ risk of bleeding Moderate	Possible displacement of protein binding	1–3 days	NR (t½ = 2–5 hours)	Avoid this drug, if possible, especially at high doses; monitor INR and monitor for bleeding		
Bosentan	↓ INR Moderate	May induce warfarin metabolism (through CYP3A4 and/or CYP2C9)	5–10 days	NR (t½ = 5–8 hours)	Monitor INR when starting or stopping bosentan; AMS considers empiric 15%–20% warfarin dose increase, with further increases according to weekly INR; may need increase in warfarin dose ofas much as 50%	2	
Carbamazepine (CBZ)	↓ INR Moderate to severe	Increase in warfarin metabolism (through CYP2C9 induction)	10–35 days	Delayed (14–40 days) (t½ = 12–17 hours)	Monitor INR closely when starting, stopping, or adjusting CBZ; increase in warfarin dose of50%–100% may be required when initiating CBZ; decrease warfarin dose by ~50% when stopping CBZ	2	
Celecoxib	↑ INR Major (especially in elderly patients)	Celecoxib is metabolized by CYP2C9 but does not inhibit or induce this isozyme	2–5 days	NR (t½ = 11 h)	Monitor INR closely when starting or stopping celecoxib; monitor for bleeding; AMS considers empiric 0%–15% warfarin dose reduction	1	
Cephalosporins (Cefamandole, cefazolin, cefoperazole, cefotetan, cefoxitin, ceftriaxone)	↑INR Moderate		Delayed		Monitor INR closely when starting or stopping Cephalosporins	2	
Chloramphenicol	↑ INR Moderate		Delayed		monitor INR, Decrease warfarin dose if necessary	2	
Cholestyramine	↓ INR Moderate	Decrease in absorption of warfarin	1–3 days	NR	Monitor INR more frequently when starting or stopping cholestyramine; avoid administering cholestyramine within 2 hours of warfarin	2	

Cimetidine	↑ INR Moderate	Decrease in warfarin metabolism	3–5 days	~1 week (t½ = 2 hours)	Monitor INR closely when starting or stopping cimetidine until INR is stable; consider changing to another H2RA or PPI instead of using cimetidine	1	
Ciprofloxacin	↑ INR Major	Unknown; may be due to CYP1A2 inhibition; interaction more prevalent among elderly patients taking multiple medications	2–5 days	2–4 days (t½ = 3–6 hours)	Monitor INR more frequently when starting or stopping ciprofloxacin; most patients will have increase in INR, but some will experience no effect; AMS considers empiric 10%–15% warfarin dose reduction	1	drug fact 2012 2014*
Cisplatin	↑ INR, ↑ risk of bleeding Major		Delayed		หากผู้ป่วยได้รับ warfarin ร่วมกับ Cisplatin โดยเฉพาะในช่วงสามวันแรกของการรับยาเคมีบำบัด ควรมีการติดตาม INR อย่างใกล้ชิด (อย่างน้อย 2 สัปดาห์หลังรับยาเคมีบำบัด) และติดตามอาการเลือดออก และปรับขนาด	1	Yano R, et al. Ann Pharmacother Oct, 2011; 45(10):e55
Citalopram	↑ risk of bleeding Moderate		Delayed	t½ = 35 hr		2	Welmoed E, et al. Arch Intern Med. 2004;164:2367-2370
Clarithromycin	↑ INR Major	Inhibition of warfarin metabolism (through CYP3A4 inhibition)	3–7 days	NR (t½ = 5–7 hours)	Monitor INR more frequently when starting or stopping clarithromycin; AMS considers empiric 15%–25% warfarin dose reduction	1	
Clopidogrel	No effect on INR, ↑ risk of bleeding Severe	Antiplatelet effects of clopidogrel combined with anticoagulant effect of warfarin impair clotting	~2 hours for antiplatelet impact	3–7 days (platelet aggregatio is irreversibly inhibited by metabolite of clopidogrel for lifetime of the platelet)	Monitor for bleeding	1	

Cloxacillin	↑ INR Moderate	Unknown	Delayed	NR (t½ = 0.5–1 hour)	Monitor INR frequently when starting or stopping cloxacillin; AMS will not empirically decrease warfarin unless patient has other factors affected INR (e.g., decreased appetite, fever)	2	
Colchicine	↑ INR Moderate	Possibly due to diarrhea associated with colchicine	1–3 days	1–3 days (t½ = 26.6–31.2 hours)	If patient is experiencing significant diarrhea with colchicine (>3–4 loose stools per day), check INR; decrease in warfarin dose may be needed during concurrent therapy with colchicine		
Cyclophosphamide	↑ INR, ↑ risk of bleeding Major	possible protein displacement, inhibition of warfarin metabolism, or inhibition of clotting-factor synthesis	Not Specified			1	Seifter et al, Cancer Treat Rep. 1985 Feb;69(2):244-245.
Danazol	↑ INR Moderate	Decrease in warfarin metabolism; may relate to direct inhibition of fibrinolytic systems	3–7 days	Delayed (t½ = 24 h)	Monitor INR when starting or stopping danazol; warfarin dose reductions of ~50% may be necessary	1	
Darunavir	↓ INR Moderate	Induction of warfarin metabolism observed with use of ritonavir (through CYP2C9, CYP1A2 induction); AUC for S-warfarin decreased by 21% when given with darunavir / ritonavir combination. Induction of warfarin metabolism likely due to ritonavir (through CYP2C9, CYP1A2 induction)	1 week	Delayed (t½ = ~15 hours)	Monitor INR more frequently when starting or stopping darunavir; warfarin dose increase of up to 20% may be required; inductive effect on warfarin may be due to coadministration of ritonavir	4	

Dextrothyroxine	↑ INR Major		Delayed		monitor INR, Decrease warfarin dose if necessary	1	
Dexamethasone	↑ INR or ↓ INR Moderate		Delayed		monitor INR, adjust warfarin dose if necessary	2	
Delavirdine	↑ INR Moderate	Possible inhibition of warfarin metabolism (through CYP3A4 inhibition)	Delayed	Several days ($t_{1/2}$ = ~ 6 hours)	Monitor INR more frequently when starting or stopping delavirdine; decrease in warfarin dosage may be required	4	
Diclofenac	No effect on INR, ↑ risk of bleeding Major	Inhibition of platelets and gastroprotective prostaglandins	2–5 days	3–7 days ($t_{1/2}$ = 2 hours)	Minimal interaction if diclofenac administered topically; minimize oral use; watch for bleeding, especially gastrointestinal bleeding	1	
Dicloxacillin	↓ INR Moderate	Increase in warfarin metabolism (through CYP2C9, CYP3A4 induction	Delayed	เริ่มเห็นการลดลงของ INR หลังจากเริ่มให้ dicloxacillin คู่กันไป 4-5 วัน และมีผลต่อเนื่องหลังหยุดยาไปแล้วอีกอย่างน้อย 2-3	monitor INR ในช่วงแรกของการให้ และ หลังจากหยุด dicloxacillin อย่างน้อยอีก 3 สัปดาห์	2	Lacey CS, Interaction of dicloxacillin with warfarin. Ann Pharmacother 2004; 38(5): 898.
Disopyramide	↑ INR Moderate	Unknown	2–5 days	2–5 days (t = 4–10 hours)	Monitor INR when starting or stopping disopyramide	5	
Doxepin	↑ INR Moderate		Delayed			2	
Doxycycline	↑ INR Major	Unknown; possible inhibition of CYP3A4-mediated warfarin metabolism and/or protein-binding displacement	2–5 days	NR ($t_{1/2}$ = 15–24 hours)	Monitor INR when starting or stopping doxycycline; AMS will not empirically decrease warfarin unless patient has other factors affecting INR (e.g., decreased appetite, fever)	1	

Dronedarone	↔ or ↑ INR Mild	Dronedarone 600 mg bid increased S-warfarin 1.2-fold via moderate inhibition of CYP3A4, INR increased 1.07-fold	3-5 days	NR (t½ = 25–30 hours; completely eliminated after 2 weeks)	No evidence of safety concerns with coadministration in clinical trials		
Efavirenz	↑ or ↓ INR Moderate to severe	Inhibition or induction of warfarin metabolism (efavirenz induces CYP3A4 and may inhibit CYP2C9)	2–3 weeks	Several weeks (t½ = 40–55 hours)	Consider empiric reduction of warfarin dose; monitor INR more frequently when starting or stopping efavirenz; one patient required 4-fold reduction in warfarin dose	4	
Erythromycin	↑ INR Major	Decrease in warfarin metabolism (through CYP3A4 inhibition)	3–5 days	3–5 days (t½ = ~1.5 hours)	Monitor INR when starting or stopping erythromycin; AMS considers empiric 10%–15% warfarin dose reduction	1	
Ethinyl estradiol	↑ or ↓ INR ↑ or ↓ anticoagulation Moderate	Unknown; case reports of substantial increase in INR after administration of emergency contraceptive pill; long-term estrogen therapy thought to be thrombogenic	2–7 days	Delayed (t½ = 13–27 hours)	Avoid concurrent use if possible; monitor INR closely; monitor clinically for signs of bruising or bleeding	4	
Etravirine	↑ INR Moderate	Inhibition of warfarin metabolism (through CYP2C9 inhibition)	1–2 weeks	1–2 weeks (t½ = 41 hours)	Consider empiric reduction of warfarin dose; monitor INR more frequently when starting or stopping etravirine		
Fibric acids (Clofibrate, Fenofibrate, Gemfibrozil see gemfibrozil)	↑ INR Major	Unknown	5–10 days	Delayed (t½ = 20–22 hours)	Monitor INR closely (i.e., weekly) when starting or stopping fenofibrate; AMS considers initial empiric 10%–15% warfarin dose reduction, in anticipation of eventual reduction of up to 40%	1	

Fluoxymesterone and other androgens (Danazol, methyltestosterone, nandrolone decanoate, oxandrolone, oxymetholone, stanozolol, testosterone)	↑ INR Major		Delayed		Avoid combination if possible. Otherwise, monitor INR and decrease warfarin dose if necessary	1	
Fluconazole	↑ INR Major	Inhibition of warfarin metabolism (via CYP2C9- and CYP3A4)	2–3 days	7–10 days (t½ = ~30 hours; prolonged in elderly patients)	Monitor INR closely when starting or stopping fluconazole; effects more pronounced in patients with reduced renal function due to reduced clearance of fluconazole; AMS considers empiric 25%–30% warfarin dose reduction, with eventual reductions approaching 80%	3	
Fluorouracil	↑ INR Major	Possible protein displacement, inhibition of warfarin metabolism or inhibition of clotting-factor synthesis	2 – 4 wk		หากใช้ยา 2 ตัวร่วมกัน ควรติดตามค่า INR ที่สัปดาห์ที่ 3 เพื่อปรับขนาดยา warfarin (จำเป็นต้องลดขนาด warfarin 20 – 70%) หลังจากนั้น เมื่อสิ้นสุดการรักษาด้วย 5-FU อาจต้องเพิ่มขนาดยาภายใน 30 วัน เพื่อให้ได้ระดับ INR ตามเป้าหมาย	1	Carabino (2002)
Fluoxetine	↑ INR or*↑ Risk bleeding Moderate		Delayed	**การเพิ่มขึ้นของ INR จะเห็นได้ชัดเจนประมาณ 1 สัปดาห์เมื่อได้รับยาร่วมกัน และจะ INR จะกลับมาปกติหลังหยุดยาประมาณ 1 สัปดาห์ หรืออาจยังสูงอยู่แม้ว่าจะหยุดให้ยา		2	**Duncan D, et al. IntClinPsychopharmacol. 1998;13(2):87-94 *Welmoed E, et al. Arch Intern Med. 2004;164:2367-2370

Fluvastatin	↑ INR Moderate	Inhibition of warfarin metabolism (via CYP2C9)	1–3 weeks	Delayed (t½ = 2.5 h)	Monitor INR when starting or stopping fluvastatin; consider alternate statin (interactions involving pravastatin and atorvastatin have not been reported)	1	
Fosamprenavir	↑ INR Moderate	Possible inhibition of warfarin metabolism (through CYP3A4 inhibition)	Delayed	Several days to weeks (t½ = ~ 7.7 hours)	Monitor INR more frequently when starting or stopping fosamprenavir; addition of ritonavir booster (CYP2C9, CYP1A2 inducer) may result in net reduction in INR; see entry for ritonavir for additional information	4	
Gemfibrozil	↑ INR Major	Inhibition of warfarin metabolism (via CYP2C9); displacement of warfarin from plasma-protein binding sites	5–7 days	Delayed (t½ = 1.3 h)	Monitor INR when starting or stopping gemfibrozil; consider empiric 10%–30% warfarin dose reduction, with ongoing monitoring (based on published case reports)	1	
Griseofulvin	↓ INR Moderate			Delayed		2	
Glyburide	↑ INR Moderate	Unknown	Delayed	Delayed (t½ = 5–10 hours)	Monitor INR closely when starting or stopping glyburide		
Hydrochlorothiazide	↓ INR Moderate			Delayed		4	
Ibuprofen	No effect,↑ risk of bleeding Major	nhibition of functioning of platelets and gastroprotective prostaglandins	~2–5 days (Delayed)	3–7 days (t½ =1.8–2.4 hours)	Monitor for bleeding (especially gastrointestinal); minimize or avoid concurrent use of ibuprofen; take with food	1	
Indinavir	↑ or ↓ INR Moderate	Inhibition of warfarin metabolism (through CYP3A4 inhibition)	Several weeks	1 week (t½ =1.4–2.2 hours)	Monitor INR more frequently when starting or stopping indinavir; paradoxical case report described unboosted indinavir leading to decrease in INR, which required 50% increase in warfarin dose37 ; addition of ritonavir booster (CYP2C9, CYP1A2 inducer) may result in net reduction in INR; see entry for ritonavir for additional information	4	

Indomethacin	Potential ↑ INR, ↑ risk of bleeding Moderate	Inhibition of platelet aggregation and gastroprotective prostaglandins	2–5 days	3–7 days (t½ = 4.5 hours)	Monitor INR with concomitant use; monitor for bleeding (especially gastrointestinal); minimize use; take with food	1	
Isoniazid	↑ INR Moderate	Inhibition of warfarin metabolism (via CYP2C9)	3–5 days	Delayed (t½ = ~1–4 hours)	Monitor INR when starting or stopping isoniazid; consider empiric 10%–15% warfarin dose reduction initially, then further reductions based on close monitoring of INR (at least weekly)	4	
Isotretinoin	↓ INR Moderate	Possible CYP-enzyme induction	Unclear	Unclear (t½ = 10–20 hours)	Monitor INR when starting or stopping isotretinoin; case reports indicate that increase in warfarin dose of 33%–50% may be required	4	
Itraconazole and ketoconazole	↑ INR Major	Inhibition of warfarin metabolism (via CYP2C9 and CYP3A4)	2–5 days	3–14 days (itraconazole t½ = 64 ± 32 hours; ketoconazole t½ = 2–12 hours)	Monitor INR closely when starting or stopping itraconazole or ketoconazole; AMS considers empiric 25%–30% warfarin dose reductions	3	
Ketorolac	↑ INR Major			Delayed		1	
Lactulose	↑ INR Moderate	Decreased intestinal absorption of vitamin K	1–3 days	Delayed	Monitor INR closely when starting or stopping lactulose		
Lansoprazole	↑ INR Moderate	Unknown	2–7 days	NR (t½ = 0.9–1.5 hours)	Monitor INR when starting or stopping lansoprazole; consider re-assessing INR in 1 week		
Leflunomide	↑ INR Major	Inhibition of warfarin metabolism (via CYP2C9)	2–10 days	Delayed (t½ = ~2 weeks)	Monitor INR closely when starting or stopping leflunomide	4	
Levofloxacin	↑ INR Major	Unknown; possible CYP1A2 inhibition; clinically significant interaction more common among elderly patients	3–5 days	5–10 days	Monitor INR closely when starting or stopping levofloxacin; INR will be affected by severity of illness; AMS considers empiric 0%–15% warfarin dose reduction	1	

Thyroid hormones (Levothyroxine, liothyronine, liotrix, thyroid)	↑ INR Moderate	Patients with hypothyroidism have higher requirements for warfarin because of decreased catabolism of clotting factors; correcting hypothyroidism therefore decreases warfarin requirements	1–2 weeks	1–2 weeks (t½ = 6–7 days)	Monitor INR closely (every 1–2 weeks) when starting or adjusting levothyroxine; adjust warfarin gradually according to INR results	1	
Lovastatin	↑ INR Major	Inhibition of warfarin metabolism		Delayed	monitor INR, adjust warfarin dose as needed when starting or stopping HMG-CoA reductase inhibitor	1	
Lopinavir/ritonavir (Kaletra)	↓ INR Moderate	Increase in warfarin metabolism (through CYP2C9, CYP1A2 induction)	Several days to weeks	Several days to weeks (t½ = 5–6 hours)	Monitor INR more frequently when starting or stopping lopinavir–ritonavir; at steady-state, induction interaction more likely to prevail, resulting in reduced INR, requiring up to a 2-fold warfarin dose increase; see also entry for ritonavir	4	
Meclofenamiate	↑ INR Major		Delayed			1	
Mefenamic acid	↑ INR Major		Delayed			1	
Mefloquine	↑ INR Major		Delayed			4	
Mesalamine	↓ INR Mild to moderate	Unknown	Delayed	NR (t½ = 0.6–1.4 hours)	Monitor INR when starting or stopping mesalamine; one patient experienced dramatic decline in INR and deep vein osis, but INR became therapeutic once mesalamine was stopped	4	

Methimazole	↓ INR Moderate	Increased catabolism of clotting factors with introduction of methimazole and return of euthyroidism increases warfarin requirements	3–10 days	1–2 weeks (t½ = 2–3 hours)	Monitor INR closely when starting, stopping, or adjusting methimazole	1	
Methyl salicylate (topical)	↑ INR, ↑ risk of bleeding Moderate	Inhibition of warfarin metabolism and platelet aggregation	Delayed	NR	Monitor INR closely; consider alternative therapy (topical capsaicin is preferred alternative)	1	
Metronidazole	↑ INR Major	Decrease in warfarin metabolism (through CYP2C9 inhibition)	3–5 days	~ 2 days (t½ = 8 hours)	Monitor INR closely when starting or stopping metronidazole; AMS considers empiric 25% –40% warfarin dose reduction	1	
Miconazole (oral, topical, or vaginal formulation)	↑ INR Moderate	Inhibition of warfarin metabolism (via CYP2C9 and CYP3A4)	2–5 days	2–5 days (t½ = 24 hours)	Monitor INR closely when starting or stopping topical, vaginal, or oral miconazole; consider alternative therapy (e.g., clotrimazole, which has no interaction with warfarin); AMS considers empiric 25%–30% warfarin dose reduction		
Moxifloxacin	↑ INR Major	Unknown; possible inhibition of CYP1A2; clinically significant interaction more common among elderly patients	2–5 days	2–3 days (t½ = ~12.7 hours)	Monitor INR closely when starting or stopping moxifloxacin; INR will be affected by severity of illness; AMS considers 0%–25% warfarin dose reduction	1	
Nalidixic acid	↑ INR Moderate		Delayed		Monitor INR. Decrease warfarin dose if necessary	2	
Norfloxacin	↑ INR Major		Delayed			1	
Nortriptyline	↑ INR Moderate		Delayed			2	ไม่พบว่ามีDI
Naproxen	No effect on INR, ↑ risk of bleeding Major	Inhibition of platelet aggregation and production of gastroprotective prostaglandins	2–5 days	3–7 days (t½ = 12–15 hours)	Monitor closely for bleeding (especially gastrointestinal); avoid or minimize concurrent use; take with food	1	

Nelfinavir	↑ or ↓ INR Moderate	Possible reduction or increase in warfarin metabolism possible (through CYP3A4 inhibition, CYP2C9 induction)	Several days	Several days (t½ = 3.5–5 hours)	Monitor INR frequently when starting or stopping nelfinavir	4	
Nevirapine	↓ INR Moderate to severe	Increase in warfarin metabolism (through CYP3A4 induction)	Several days to weeks	Several days to weeks (t½ = 45 hours)	Monitor INR more frequently when starting or stopping nevirapine; 2- to 4-fold increase in warfarin dose may be required (based on case reports)	2	
Ofloxacin	↑ INR Major	Metabolism/transport effectsInhibits CYP1A2 (strong)	Delayed	การเพิ่มฤทธิ์ของยา warfarin จะเห็นได้ชัดเจนภายในวันที่ 3-4 และขึ้นสูงสุดภายในระยะเวลาไม่เกิน 2 สัปดาห์ (7-14 วัน) และเมื่อหยุดยาการตอบสนองของ hypoprothrombinemic จะกลับสู่สภาวะปกติ		1	Leor J, et a.lAnn Intern Med. 1988;109:761
Omeprazole	↑ INR Mild to moderate	Decrease in warfarin metabolism through stereoselective inhibition of the hepatic metabolism of the less potent (R)-warfarin enantiomer	3–5 days	NR (t½ = 0.5–1 hour)	Interaction of doubtful clinical significance; minimal effect on INR; no empiric warfarin dose adjustment required	4	
Orlistat	↑ INR Moderate	Decreased absorption of fat-soluble vitamins, including vitamin K	Unknown	NR	Monitor INR closely with concomitant use; avoid concomitant use if possible		
Paroxetine	↑ in risk of bleeding		Delayed			2	Welmoed E, et al. Arch Intern Med. 2004;164:2367-2370
Penicillins	↑ INR Moderate		Delayed		monitor INR, Decrease warfarin dose if necessary	2	
Piroxicam	↑ INR Major		Delayed			1	

Phenytoin	Initially, transient ↑ in risk of bleeding; with long-term use, ↓ INR 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 (t½ = 22 hours)	Monitor INR closely when starting or stopping phenytoin; AMS recommends no empiric dose adjustment when phenytoin is initiated, but monitoring of INR at least weekly; some patients may require up to 50% warfarin dose increase several weeks after phenytoin is initiated; warfarin also affects phenytoin concentration	2	
Prednisone	↑ or ↓ INR Moderate	Unknown	Delayed	NR (t½ = 2.6–3 hours)	Monitor INR when starting or stopping prednisone; AMS recommends no empiric dose adjustment when initiating prednisone; warfarin dose adjustment may be required for patients receiving large bolus or pulse doses of steroids; monitor for bleeding	2	
Propafenone	↑ INR Moderate	Decrease in warfarin metabolism; 39% increase in plasma concentration of warfarin reported	2–5 days	~2 days (t½ = 2–10 h)	Monitor INR when starting or stopping propafenone; AMS empirically reduces warfarin dose by 15%–30% and monitors closely, with futher reductions as required	4	
Propoxyphene	↑ INR Moderate	Unknown (may be due to propoxyphene alone or to acetaminophen component when used in combination)	Delayed	NR (t½ = 2.6–3 hours)	Monitor INR when starting or stopping propoxyphene (based on published case reports only)	4	
Propylthiouracil	↓ INR Moderate	Increased catabolism of clotting factors with introduction of propylthiouracil and return of euthyroidism increases requirement for warfarin	Within 2 weeks	1–2 weeks (t½ = 1.5–5 hours)	Monitor INR closely when starting, stopping, or adjusting dose of propylthiouracil	1	

Quinine derivatives (Q	↑ INR Major		Delayed		monitor INR. Decrease warfarin dose if necessary	1	
Quetiapine	↑ INR Moderate	Competitive inhibition of CYP3A4 and CYP2C9	7–14 days	NR (t½ = ~6 h)	Monitor INR when starting or stopping quetiapine (based on single case report only)		
Raloxifene	↓ INR Moderate (based on single-dose tudies only; no data on long-term use)	Unknown	Rapid	NR (t½ = 27 hours)	Monitor INR closely when starting or stopping raloxifene		
Ranitidine	↑ INR Moderate	Inhibition of hepatic metabolism of warfarin	1–2 weeks	3–7 days (t½ = 1.9–3 hours)	Monitor INR when starting or stopping ranitidine; consider using famotidine or nizatidine instead of ranitidine	2	
Ribavirin	↓ INR Moderate	Unknown	2–4 weeks	2–4 weeks (t½ = 298 hours)	Monitor INR frequently when initiating or discontinuing ribavirin in patients taking warfarin until INR	4	
Rifampin	↓ INR Moderate to severe	Induction of hepatic metabolism of warfarin	1–3 weeks	1–5 weeks (t½ = 1.5–5 hours)	Monitor INR carefully (at least weekly) when starting or stopping rifampin; AMS considers empiric 25%–50% warfarin dose increase initially, with further increases based on frequent monitoring of INR (at least weekly); patients may require 2–3 times their regular weekly warfarin dose when rifampin is added	2	

Ritonavir	↑ or ↓ INR Moderate	Induction of warfarin metabolism (through CYP2C9, CYP1A2 induction)	Several days to weeks	1 week (t½ = 3–5 hours)	Monitor INR more frequently when starting or stopping ritonavir; up to 2-fold increase in warfarin dose and 3-fold increase in acenocoumarol dose documented in case reports; another case report documented the opposite effect (increased INR requiring vitamin K and decrease in warfarin dose); see also entry for lopinavir–ritonavir	2	
Ropinirole	↑ INR Severe	Competitive inhibition of CYP1A2-mediated warfarin metabolism and/ or displacement of warfarin from binding sites	5–10 days	NR (t½ = 6 hours)	Monitor INR closely when starting or stopping ropinirole (based on single published case report)	4	
Rosuvastatin	↑ INR Major	Unknown	3–7 days	3–7 days ((t½ = 19 hours)	Monitor INR when starting or stopping rosuvastatin; consider alternative statin (no reports of interaction with warfarin for atorvastatin or pravastatin); AMS empirically reduces warfarin dose by 10%–25% and reassesses INR within 1 week	1	
Rofecoxib	↑ INR Major		Delayed			1	
Saquinavir	↑ INR Moderate	Decrease in warfarin metabolism (through CYP3A4 inhibition)	Up to 4–8 weeks	3–7 days (t½= 13 hours)	Consider empiric decrease in warfarin dose with use of unboosted saquinavir; monitor INR more frequently when starting or stopping saquinavir; one patient required a 20% decrease in warfarin dose with unboosted saquinavir; addition of ritonavir booster (CYP2C9, CYP1A2 inducer) may result in net decrease in INR; see entry for ritonavir for additional information	4	

Secobarbitol	↓ INR Major		Delayed			1	
Selegiline	↑ INR Moderate	Selegiline มีผลยับยั้งการทำงานของ CYP1A2 (ระดับ moderate) , CYP2C9 และ CYP3A4 (ระดับ weak)	Delayed	t½ = 10 hr		4	Christopher R. Ensor and Stacey R. Dean. Hosp Pharm. 2010; 45(6):478–483.
Sertraline	↑ INR Moderate	unknown: serotonin (5-HT) มีบทบาทสำคัญในการกระตุ้นให้เกิดกระบวนการ platelet aggregation ช่วยทำให้เลือดหยุดไหล และยาในกลุ่ม SSRIs มีผลยับยั้งการเก็บกลับสารสื่อประสาท serotonin ดังนั้นการลดลงของ serotonin จึงอาจจะส่งผลให้เพิ่มความเสี่ยงในการเกิดเลือดออกได้	Delayed	t½ = sertraline 26 hr, N-desmethylsertraline 66 hr		2	Welmoed E, et al. Arch Intern Med. 2004;164:2367-2370
Simvastatin	↑ INR Major	Competition for CYP3A4-mediated metabolism	3–7 days	3–7 days (t½ = 3 hours)	Monitor INR when starting or stopping simvastatin; interaction may range from negligible to clinically significant; consider using alternative statin (atorvastatin or pravastatin)	1	
Sulindac	↑ INR Major		Delayed			1	
Sulfonamides (sulfamethizole, sulfamethoxazole with or without trimethoprim, sulfasalazine, sulfisoxazole)	↑ INR Major	Inhibition of warfarin metabolism and displacement of warfarin from protein-binding sites	2–5 days	2–14 days (t½ of sulfamethoxazole = 10 hours)	Monitor INR closely when starting or stopping sulfamethoxazole-containing drug regimens; AMS considers empiric 25%–40% warfarin dose reduction	1	

Sulfasalazine	↓ INR or ↑ INR Major	Unknown	Unknown	NR (t½ = ~7.6 hours)* ค่า INR เพิ่มเป็น 6.1 (เพิ่มขึ้น 3 เท่า หลังให้ยา Sulfasalazine 3 wk)เมื่อ	Monitor INR frequently when starting or stopping sulfasalazine; one patient required 250% increase in weekly warfarin dose when sulfasalazine was started	1	*Hall S1, Rindone JP. J Clin Pharm Ther. 2011 Apr;36(2):246-8.
Sulfinpyrazone	↑ INR Moderate	Inhibition of warfarin metabolism (primarily S-isomer)	Delayed	1–2 weeks (t½ = 4–4.3 hours)	Monitor INR when starting or stopping sulfinpyrazone; average daily warfarin dose decreased by ~50% in small case series	1	
Tamoxifen	↑ INR Major		Delayed (3-6 wk)		ปฏิกิริยานี้โดยทั่วไปอยู่ในระดับรุนแรง และมีแนวโน้มจะเป็นชนิดที่ขึ้นกับขนาดยา warfarin ดังนั้นจึงควรมีการติดตามระดับ PT/INR อย่างน้อย 1-3 วันหลังได้รับยาทั้ง 2 ตัวร่วมกัน	1	Lodwick R et al.Br Med J 1987;295: 1141. Mishra D, Paudel R, Kishore PV, Palaian S, Bista
Thyroid hormones (Levothyroxine, liothyronine, liotrix, thyroid)	↑ INR Moderate	Patients with hypothyroidism have higher requirements for warfarin because of decreased catabolism of clotting factors; correcting hypothyroidism therefore decreases warfarin requirements	1–2 weeks	1–2 weeks (t½ of levothyroxine = 6–7 days)	Monitor INR closely (every 1–2 weeks) when starting or adjusting thyroid hormone; adjust warfarin gradually according to INR results	1	
Terbinafine	Both ↑ and ↓ INR have been reported Moderate	Unknown	Unknown	NR (t½ = 36 hours)	Monitor INR when starting or stopping terbinafine	4	
Tetracycline	↑ INR Major	Reduced plasma prothrombin activity	2–5 days	NR (t½ ~8–10 hours)	Monitor INR	1	
Ticlopidine	↑ INR, ↑ risk of bleeding Moderate	Inhibition of metabolism of R-warfarin (minimal increase in INR); decreased platelet aggregation	1–5 days	3–7 days for platelet function to return to baseline	Monitor INR when starting or stopping ticlopidine; monitor for increased bleeding (patient may be at risk even if INR if INR does not increase)	1	

Tipranavir	↔ or ↓ INR Mild	Possible increase in warfarin metabolism (through CYP3A4 induction); however manufacturer predicts ↔ on S-warfarin concentration	Delayed	Several days to weeks (t½ = 5.5–6 hours)	Monitor INR more frequently when starting or stopping tipranavir; addition of ritonavir booster (CYP2C9, CYP1A2 inducer) may result in net decrease in INR; use caution when combining with warfarin, as tipranavir has been associated with increased risk of intracranial hemorrhage; see entry for ritonavir for additional information		
Tramadol	↑ INR Moderate	Unknown (possible inhibition of CYP3A4-mediated warfarin metabolism)	3–7 days	3–7 days (t½ = 5.6–6.7 hours)	Monitor INR when starting or stopping tramadol; dose reductions of 25%–30% may be required; AMS considers empiric 0%–20% warfarin dose reduction	2	
Vitamin E	↑ INR Major		Delayed		monitor INR. Decrease warfarin dose if necessary	1	
Vitamin K	↓ INR Moderate		Delayed		Avoid or minize intake of foods with high vitamin K. Monitor INR. Adjust warfarin dose as needed.	2	
Voriconazole	↑ INR Major	Inhibition of CYP2C9-mediated metabolism of S-warfarin	3–7 days	NR (t½ = 6 hours)	Monitor INR carefully when starting or stopping voriconazole; AMS considers empiric 25%–30% warfarin dose reduction	3	
AMS= Anticoagulant management service t1/2 = half life NR= Not report							

Ref: Drug Interaction Fact 2012

C.A., The potential effects of dicloxacillin on warfarin	AT, et al. Potential interaction between warfarin