

Drug Interaction Considerations With Coumadin[®] (Warfarin Sodium)

Prothrombin time (PT) determinations/INR are used to measure the patient's response to warfarin therapy. However, numerous factors, alone or in combination, can influence the prothrombin time response of the patient to warfarin (eg, travel, changes in diet, environment, physical state, and medication). Consequently, it is generally good practice to monitor the patient's response with additional prothrombin time determinations in the period immediately after discharge from the hospital, and whenever other medications are initiated, discontinued, or taken irregularly.

Drugs may interact with Coumadin[®] through pharmacodynamic or pharmacokinetic mechanisms. Pharmacodynamic mechanisms for drug interactions with Coumadin[®] are synergism (impaired hemostasis, reduced clotting factor synthesis), competitive antagonism (vitamin K), and altered physiologic control loop for vitamin K metabolism (hereditary resistance). Pharmacokinetic mechanisms for drug interactions with Coumadin[®] are mainly enzyme induction, enzyme inhibition, and reduced plasma protein binding. It is important to note that some drugs may interact by more than one mechanism.

Because a patient may be exposed to a combination of factors (eg, travel, changes in diet, environment, physical state, medication), the net effect of Coumadin[®] on PT/INR response may be unpredictable. More frequent PT/INR monitoring is therefore advisable. Medications of unknown interaction with coumarins are best regarded with caution. When these medications are started or stopped, more frequent PT/INR monitoring is advisable. Please see accompanying Full Prescribing Information on Coumadin[®].

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OTHER FACTORS THAT MAY AFFECT PROTHROMBIN TIMES/INR

DECREASED PT/INR	INCREASED PT/INR
	<ul style="list-style-type: none"> • Other medications affecting blood elements which may modify hemostasis • Blood dyscrasias • Cancer • Collagen vascular disease • Congestive heart failure • Diarrhea • Diet high in vitamin K • Dietary deficiencies • Edema • Elevated temperature • Hepatic disorders: <ul style="list-style-type: none"> • Infectious hepatitis • Jaundice • Hereditary coumarin resistance • Hyperlipemia • Hypothyroidism • Nephrotic syndrome • Poor nutritional state • Prolonged hot weather • Steatorrhea • Unreliable PT/INR determinations[†] • Vitamin K deficiency

Because a patient may be exposed to a combination of the above factors, the net effect of Coumadin® on PT/INR response may be unpredictable. More frequent PT/INR monitoring is therefore advisable. Medications of unknown interaction with coumarins are best regarded with caution. When these medications are started or stopped, more frequent PT/INR monitoring is advisable.

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ONLY FROM 
COUMADIN[®] *Today*
 (Warfarin Sodium Tablets, USP) Crystalline
 (Warfarin Sodium for Injection, USP)
 MOVING BEYOND ITS TRADITIONAL ROLE

**DU PONT
 PHARMA**

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DECREASED PT/INR	INCREASED PT/INR	SPECIFIC DRUGS REPORTED
	•	Dextran
	•	Dextrothyroxine
	•	Diazoxide
	•	Diclofenac
•		Dicloxacillin
	•	Dicumarol
	•	Diffunisal
	•	Disulfiram
	•	Doxycycline
	•	Erythromycin
	•	Ethacrynic acid
•		Ethchlorvynol
	•	Fenoprofen
	•	Fluconazole
	•	Fluorouracil
	•	Fluoxetine
	•	Fluvoxamine
	•	Glucagon
•		Glutethimide
•		Griseofulvin
•		Haloperidol
	•	Halothane
	•	Heparin
	•	Ibuprofen
	•	Ifosfamide
	•	Indomethacin
	•	Influenza virus vaccine
	•	Itraconazole
	•	Ketoprofen
	•	Ketorolac
	•	Levamisole
	•	Levothyroxine
	•	Liothyronine
	•	Lovastatin
	•	Mefenamic acid
•		Meprobamate
•		6-Mercaptopurine
•		Methimazole [†]
	•	Methyldopa
	•	Methylphenidate
	•	Methylsalicylate ointment, topical
	•	Metronidazole
	•	Miconazole
•		Moricizine HCl [†]
•		Nafcillin
	•	Nalidixic acid
	•	Naproxen
	•	Neomycin
	•	Norfloxacin
	•	Ofloxacin

DECREASED PT/INR	INCREASED PT/INR	SPECIFIC DRUGS REPORTED
	•	Olsalazine
	•	Omeprazole
	•	Oxaprozin
	•	Oxymetholone
•		Paraldehyde
	•	Paroxetine
	•	Penicillin G, intravenous
•		Pentobarbital
	•	Pentoxifylline
•		Phenobarbital
•		Phenylbutazone
•		Phenytoin [†]
	•	Piperacillin
	•	Piroxicam
•		Prednisone[†]
•		Primidone
	•	Propafenone
	•	Propoxyphene
	•	Propranolol
•		Propylthiouracil [†]
	•	Quinidine
	•	Quinine
•		Ranitidine [†]
•		Rifampin
•		Secobarbital
	•	Sertraline
	•	Simvastatin
•		Spirolactone
	•	Stanozolol
•		Streptokinase
•		Sucralfate
	•	Sulfamethizole
	•	Sulfamethoxazole
	•	Sulfinpyrazone
	•	Sulfisoxazole
	•	Sulindac
	•	Tamoxifen
	•	Tetracycline
	•	Thyroid
	•	Ticarcillin
	•	Ticlopidine
	•	Tissue plasminogen activator (t-PA)
	•	Tolbutamide
•		Trazodone
	•	Trimethoprim/sulfamethoxazole
	•	Urokinase
	•	Valproate
•		Vitamin C, high dose
	•	Vitamin E
•		Vitamin K

[†]Both increased and decreased PT/INR responses have been reported.

Because a patient may be exposed to a combination of the above factors, the net effect of Coumadin® (Warfarin Sodium) on PT/INR response may be unpredictable. More frequent PT/INR monitoring is therefore advisable. Medications of unknown interaction with coumarins are best regarded with caution. When these medications are started or stopped, more frequent PT/INR monitoring is advisable.

DRUG INTERACTION CONSIDERATIONS WITH COUMADIN® (Warfarin Sodium)

DECREASED PT/INR	INCREASED PT/INR	CLASSES OF DRUGS
•		Adrenal cortical steroid inhibitors†
	•	Adrenergic stimulants, central
	•	Alcohol abuse reduction preparations
	•	Analgesics
	•	Anesthetics, inhalation
•		Antacids
•		Antianxiety agents
•	•	Antiarrhythmics†
•	•	Antibiotics†
		Aminoglycosides, oral
		Cephalosporins, parenteral
		Macrolides
		Miscellaneous
		Penicillins, intravenous, high dose
		Quinolones, fluoroquinolones
		Sulfonamides, long acting
		Tetracyclines
	•	Anticoagulants
•	•	Anticonvulsants†
•	•	Antidepressants†
•		Antihistamines
	•	Antimalarial agents
•	•	Antineoplastics†
	•	Antiparasitic/antimicrobials
	•	Antiplatelet drugs/effects
•		Antipsychotic medications
•	•	Antithyroid drugs†
•		Barbiturates
	•	Beta-adrenergic blockers
	•	Bromelains
	•	Cholelitholytic agents
	•	Diabetes agents, oral
•	•	Diuretics†
•		Enteral nutritional supplements
•	•	Fungal medications, systemic†
•	•	Gastric acidity and peptic ulcer agents†
	•	Gastrointestinal, ulcerative colitis agents
	•	Gout treatment agents
	•	Hemorrhologic agents
	•	Hepatotoxic drugs
	•	Hyperglycemic agents
	•	Hypertensive emergency agents
•	•	Hypnotics†
•	•	Hypolipidemics†
•		Immunosuppressives
	•	Monoamine oxidase inhibitors
	•	Narcotics, prolonged
	•	Nonsteroidal anti-inflammatory agents
•	•	Oral contraceptives, estrogen containing
	•	Psychostimulants
	•	Pyrazolones

DECREASED PT/INR	INCREASED PT/INR	CLASSES OF DRUGS
	•	Salicylates
	•	Selective serotonin reuptake inhibitors
•	•	Steroids, adrenocortical†
	•	Steroids, anabolic (17-alkyl testosterone derivatives)
	•	Thrombolytics
	•	Thyroid drugs
•	•	Tuberculosis agents†
	•	Uricosuric agents
	•	Vaccines
•	•	Vitamins†

SPECIFIC DRUGS REPORTED

DECREASED PT/INR	INCREASED PT/INR	SPECIFIC DRUGS REPORTED
	•	Acetaminophen
•	•	Alcohol†
	•	Allopurinol
•		Aminoglutethimide
	•	Aminosalicic acid
	•	Amiodarone HCl
•		Amobarbital
	•	Aspirin
•		Azathioprine
	•	Azithromycin
•		Butabarbital
•		Butalbital
•		Carbamazepine
	•	Cefamandole
	•	Cefazolin
	•	Cefoperazone
	•	Cefotetan
	•	Cefoxitin
	•	Ceftriaxone
	•	Chenodiol
•	•	Chloral hydrate†
	•	Chloramphenicol
•		Chlordiazepoxide
	•	Chlorpropamide
•		Chlorthalidone
•	•	Cholestyramine†
	•	Cimetidine
	•	Ciprofloxacin
	•	Clarithromycin
	•	Clofibrate
•		Corticotropin
•		Cortisone
	•	COUMADIN® overdose
•		COUMADIN® underdosage
•	•	Cyclophosphamide†
	•	Danazol

†Both increased and decreased PT/INR responses have been reported.