

# CAUSES OF AN INCREASED INR

Factors That May Affect INR	
Adherence	Complex regimen Splitting tablets Dosing error or duplication Multiple tablet strengths
Drug Therapy Changes	Warfarin dose recently altered Recent antibiotic use OTC or herbal product added, deleted, or dose altered Medication added, deleted, or dose altered
Lifestyle Changes	Increase in alcohol use or binge drinking Decrease in consumption of Vitamin K containing foods Chewing tobacco use recently decreased or discontinued

Warfarin-Drug Interactions That May Result in an Increased INR			
	Drug	Mechanism	Clinical Management
<b>MAJOR</b>	Antifungal agents SMZ-TMP (Bactrim)	Inhibits warfarin metabolism	<ul style="list-style-type: none"> <li>Monitor INR when azole antifungals or SMZ-TMP is added or withdrawn.</li> <li>Avoid concomitant use whenever possible.</li> </ul>
	Aspirin, Clopidogrel	Inhibits platelet aggregation	<ul style="list-style-type: none"> <li>If possible, avoid concomitant use of warfarin + ASA/Clopidogrel.</li> <li>If aspirin is needed, use a low dosage (325 mg or less).</li> </ul>
	Pradaxa, Xarelto, LMWH	Interrupts clotting cascade	<ul style="list-style-type: none"> <li>Concomitant use may increase the risk of major, life-threatening bleeding events due to additive anticoagulant effects.</li> </ul>
	Tamoxifen	Unknown	<ul style="list-style-type: none"> <li>Avoid this combination when possible.</li> <li>Monitor INR closely with the addition and withdrawal of drug.</li> </ul>
	Amiodarone	Inhibits warfarin metabolism	<ul style="list-style-type: none"> <li>A 25% reduction in the warfarin is recommended when amiodarone is initiated; monitor INR closely.</li> <li>Effect may persist for 1 to 3 months after stopping amiodarone.</li> </ul>
<b>MODERATE</b>	Acetaminophen	Inhibits warfarin metabolism	<ul style="list-style-type: none"> <li>Advise patient to maintain a steady dosage of less than 2 g per day; if higher dosages are used, increase monitoring.</li> </ul>
	Ethanol	Inhibits warfarin metabolism	<ul style="list-style-type: none"> <li>Caution patients to drink in moderation; avoid binge drinking.</li> </ul>
	H-2 Blockers Macrolide Antibiotics Metronidazole Protease Inhibitors Quinolone Antibiotics SSRI Antidepressants Statins and Fibrates Tricyclic Antidepressants	Inhibits warfarin metabolism	<ul style="list-style-type: none"> <li>Monitor INR closely when these medications are added, discontinued, or dose is altered.</li> </ul>
	Acarbose	Increases warfarin absorption	<ul style="list-style-type: none"> <li>Monitor INR when acarbose is added or withdrawn.</li> </ul>
	Lactulose	Potentialiation of anticoagulation	<ul style="list-style-type: none"> <li>Monitor INR closely with the addition and withdrawal of lactulose.</li> </ul>
	Phenytoin	Decreases warfarin protein binding, leading to increased free warfarin	<ul style="list-style-type: none"> <li>Monitor INR closely during the two to three week interval following the addition or deletion of phenytoin therapy. (<i>Initial increase in warfarin effect, then a decrease in effect after prolonged use.</i>)</li> </ul>
	Thyroid hormones	Interferes with clotting factors	<ul style="list-style-type: none"> <li>Monitor INR frequently for 1 to 2 months after thyroid medication adjustments.</li> </ul>
	Vitamin E		<ul style="list-style-type: none"> <li>INR effects more likely to occur with Vitamin E &gt;800 IU per day</li> </ul>
	NSAIDs, Cox-2 inhibitors	Inhibit platelet aggregation	<ul style="list-style-type: none"> <li>Advise patients to avoid NSAIDs or to use them intermittently.</li> </ul>
	Allopurinol Influenza Vaccine Tramadol Oxandrolone	Unknown	<ul style="list-style-type: none"> <li>Monitor INR when medication is added, removed or dose is altered.</li> <li>Monitor INR within one to two weeks following the influenza vaccine.</li> </ul>

Reference:Thompson Micromedex, 2012

The information in this publication is provided in summary form. It is not intended for use as the sole basis of clinical treatment, as a substitute for reading the original research, not as a substitute for the knowledge, skill, or judgment of the medical provider. This guide presents only a sample of possible explanations for an increased INR.

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# CAUSES OF A DECREASED INR

Factors That May Affect INR	
<b>Adherence</b>	Complex regimen Splitting tablets Dosing error or duplication Multiple tablet strengths
<b>Drug Therapy Changes</b>	Warfarin dose recently altered Recent antibiotic use OTC/herbal product added, deleted, or dose altered Medication added, deleted, or dose altered
<b>Lifestyle Changes</b>	Decrease in baseline alcohol use Increase in consumption of Vitamin K containing foods Chewing tobacco recently started or frequency of use increased

Warfarin-Drug Interactions That May Result in a Decreased INR			
	Drug	Mechanism	Clinical Management
<b>MAJOR</b>	<b>Phenobarbital and other barbiturates</b>	Increases warfarin metabolism	<ul style="list-style-type: none"> <li>If concurrent therapy is required, monitor INR closely when drugs are initiated, discontinued or when a dose is changed.</li> <li>Phenytoin: There may be an initial increase in warfarin effect (due to altered binding), then a decrease in warfarin effect (due to increased warfarin metabolism) after prolonged use.</li> </ul>
	<b>Phenytoin</b>		
	<b>St. Johns Wort</b>		
<b>MODERATE</b>	<b>Azathioprine</b>	Decreases warfarin absorption	<ul style="list-style-type: none"> <li>Monitor INR closely when these drugs are initiated, discontinued or when a dose is changed.</li> <li>Consider separating administration of sucralfate, colestipol, or cholestyramine from warfarin dose by 2 hours.</li> </ul>
	<b>Cholestyramine</b>		
	<b>Colestipol</b>		
	<b>Estrogens</b>		
	<b>Soy</b>		
	<b>Sucralfate</b>		
	<b>Carbamazepine</b>	Increases warfarin metabolism	<ul style="list-style-type: none"> <li>Monitor the INR closely when these drugs are initiated, discontinued or when a dose is changed.</li> </ul>
	<b>Dicloxacillin, Nafcillin</b>		
	<b>Primidone</b>		
	<b>Rifampin</b>		
	<b>Ginseng</b>	Unknown	<ul style="list-style-type: none"> <li>Monitor INR closely when these products are initiated, discontinued or a dose is changed.</li> <li>Instruct the patient to keep the amount of supplements in their diet as constant as possible.</li> </ul>
	<b>Griseofulvin</b>		
<b>Vitamin C (&gt;500mg/day)</b>			
<b>Spirolactone</b>	Increased concentration of clotting factors	<ul style="list-style-type: none"> <li>Monitor INR closely when drug is initiated, discontinued or a dose is changed.</li> </ul>	
<b>CoEnzyme Q10</b>	Antagonism of warfarin's mechanism of action	<ul style="list-style-type: none"> <li>Monitor the INR closely when these products are initiated, discontinued or a dose is changed.</li> <li>Instruct the patient to keep the amount of supplements in their diet as constant as possible.</li> </ul>	
<b>Green tea</b>			
<b>Vitamin K</b>			

Reference: Micromedix Database 2012

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