

The 8 A's - Drugs that interact with Warfarin*

*This is only a partial list of drugs that can alter the response to warfarin. Of note, some patients exposed to specific drug combinations will exhibit no interaction, in part because pharmacogenetics and other factors govern the expression of many interactions.

| Drug or drug class | Risk of bleeding | Mechanism |
|--|------------------|---|
| Antibiotics Most agents, but especially co-trimoxazole, metronidazole, macrolides & quinolones | ↑ | Inhibition of vitamin K synthesis by intestinal flora, inhibition of hepatic warfarin metabolism, or both |
| Rifampin | ↓ | Induction of cytochrome P450 (CYP) isoenzyme 2C9 |
| Antifungals Fluconazole, miconazole | ↑ | Inhibition of CYP 2C9 |
| Antidepressants Selective serotonin reuptake inhibitors (SSRI) | ↑ | Interference with primary hemostasis; some (e.g., fluoxetine) also inhibit CYP 2C9 |
| Antiplatelet agents ASA, clopidogrel, ticlopidine | ↑ | Interference with primary hemostasis |
| Amiodarone | ↑ | Inhibition of CYP 2C9 |
| Anti-inflammatory agents All, NSAID, including COX-2 inhibitors | ↑ | Direct mucosal injury; interference with primary hemostasis may also play a role |
| Acetaminophen | ↑ | Direct interference with vitamin K cycle |
| Alternative remedies Ginkgo, dong quai, fenugreek, chamomile | ↑ | Multiple and often incompletely characterized |
| St. John's wort | ↓ | Multiple and often incompletely characterized |

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Management of Elevated INR Associated with Warfarin Therapy

Chest 2008; 133:160S ACCP Antithrombotic Therapy Guidelines

| Conditions | Recommendations |
|--|---|
| INR <5 and with no significant bleeding | Lower the dose OR omitting a dose, monitoring more frequently, and resuming therapy at an adjusted dose when INR is at a therapeutic level. |
| INR \geq 5 but <9 and no significant bleeding. | Omit the next 1-2 doses, monitoring more frequently, and resuming therapy at an adjusted dose when the INR is at a therapeutic level. |
| With higher risk for bleeding | OR |
| | Omitting a dose, administering low dose vitamin K, 1-2.5mg orally. Expect reduction in INR within 24 hrs. Repeat vitamin K 1-2mg orally if needed. |
| INR \geq 9 and no significant bleeding. | Hold warfarin, administer higher dose of vitamin K, 2.5-5mg. Expect INR reduction within 24-48 hrs. Monitor more frequently, administer additional vitamin K if necessary. Resume therapy at an adjusted dose when INR reaches the therapeutic range. |
| Serious bleeding, with elevated INR regardless of magnitude | Hold warfarin, administer vitamin K 10mg by slow IV infusion, supplement with FFP, prothrombin complex concentrate (PCC) or recombinant factor VIIa. Repeat vitamin K every 12 hours for persistent INR elevation. |
| Life-threatening bleeding (eg, intracranial hemorrhage) and elevated INR regardless of magnitude | Hold warfarin and administer, FFP, PCC or recombinant factor VIIa, supplement with vitamin K 10mg by slow IV infusion, repeat if necessary. |



This material was prepared by the Kansas Foundation for Medical Care, Inc. (KFMC), the Medicare Quality Improvement Organization for Kansas, under contract with the Centers for Medicare & Medicaid Services (CMS), an agency of the U.S. Department of Health and Human Services. The contents presented do not necessarily reflect CMS policy. #9SOW-KS-PS_DS-09-09

