

## **DRUGS TO WATCH WITH WARFARIN**

This guide is intended as a quick reference to highlight significant interactions between Warfarin and commonly prescribed and OTC medicines. It is not intended to be exhaustive or give detailed information. For further information, prescribers should refer to the SPCC, BNF or resources offering specialised information on drug interactions. Alternatively, queries can be forwarded to the prescribing support team **or** Drug Information at either Antrim Hospital (medicines.info@uh.n-i.nhs.uk) or the Royal Victoria Hospital (nirdic@royalhospitals.n-i.nhs.uk).

The guide also provides information on interactions between Warfarin and commonly used herbal and vitamin supplements.

Where concomitant use is required, close monitoring is essential and the dose adjusted where necessary.

**Note: Please use the medicine's generic name when using the following lists.**

### **Drugs which increase anticoagulant effects of Warfarin**

<b>Interacting Drug</b>	<b>Additional Comment</b>
<b>Alcohol</b>	Fluctuations in INR particularly in heavy drinkers or those with liver disease
<b>Allopurinol</b>	Anticoagulant effects possibly enhanced – monitor closely
<b>Amiodarone</b>	Slow onset – may persist long after Amiodarone is stopped. Monitor closely
<b>Amitriptyline</b>	Can cause unpredictable increases or decreases in INR – monitor closely
<b>Aspirin</b>	Avoid Aspirin as analgesic, use Paracetamol as safer alternative. Low dose Aspirin 75-100mg appears not to interact significantly
<b>Azapropazone</b>	Significant – avoid concomitant use
<b>Bezafibrate</b>	Reduce Warfarin dose by one third to a half initially and adjust accordingly – monitor closely
<b>Cefaclor</b>	Cefalexin, Cefradine and Cefuroxime are safer alternatives
<b>Celecoxib</b>	Rare cases of increased INR and bleeding – monitor closely
<b>Ciprofibrate</b>	Reduce Warfarin dose by one third to a half initially and adjust accordingly – monitor closely
<b>Ciprofloxacin</b>	Rare but unpredictable - monitor
<b>Clarithromycin</b>	Serious interaction but unpredictable and uncommon - use azithromycin as alternative
<b>Clopidogrel</b>	Increased risk of bleeding due to antiplatelet effect (Manufacturer advises avoid concomitant use)
<b>Dexamethasone</b>	May enhance or reduce Warfarin effects - high doses enhance
<b>Dextropropoxyphene</b>	Rare but unpredictable – monitor closely
<b>Diclofenac</b>	Increased bleeding risk with oral Diclofenac. Increased risk of haemorrhage with IV diclofenac - avoid concomitant use
<b>Dipyridamole</b>	Increased risk of mild bleeding due to antiplatelet effect
<b>Erythromycin</b>	Serious but unpredictable. Elderly at greatest risk. Monitor closely

<b>Esomeprazole</b>	Anticoagulant effects possibly enhanced – interactions do not appear to be clinically significant. Monitor
<b>Fenofibrate</b>	Reduce Warfarin dose by one third to a half initially and adjust accordingly – monitor closely
<b>Fluoxetine</b>	Isolated reports of raised INR and/or haemorrhage - monitor
<b>Fluvastatin</b>	May increase anticoagulant effects - monitor
<b>Ibuprofen</b>	Anticoagulant effects possibly enhanced – monitor closely
<b>Influenza vaccine</b>	Anticoagulant effects possibly enhanced – monitor closely
<b>Itraconazole</b>	Isolated reports but clinically significant – monitor closely
<b>Ketoconazole</b>	Monitor closely – especially in elderly
<b>Lansoprazole</b>	Anticoagulant effects possibly enhanced although interactions do not appear to be clinically significant. Monitor
<b>Mefenamic acid</b>	Anticoagulant effects possibly enhanced – monitor closely
<b>Metronidazole</b>	Avoid where possible. Warfarin dose may need to be reduced by up to half. Monitor closely
<b>Miconazole</b>	Avoid – potentially serious interaction. Use nystatin where possible
<b>Mirtazepine</b>	Anticoagulant effect enhanced – monitor and adjust dose
<b>Ofloxacin</b>	Rare but unpredictable - monitor
<b>Omeprazole</b>	Anticoagulant effects possibly enhanced – occasionally clinically significant interactions occur. Monitor
<b>Orlistat</b>	Manufacturer recommends monitoring of Warfarin dose/INR
<b>Paracetamol</b>	Intermittent analgesic use unlikely to affect INR (less than 2.5g/week) Prolonged regular use of high doses have been found to increase INR
<b>Penicillin(s)*</b>	See below*
<b>Phenytoin</b>	May reduce or enhance anticoagulant effects – monitor closely
<b>Piroxicam</b>	Monitor and reduce dose if necessary
<b>Prednisolone</b>	May enhance or reduce Warfarin effects -high doses enhance
<b>Propafenone</b>	Monitor and reduce dose if necessary
<b>Rosuvastatin</b>	Anticoagulant effect possibly enhanced – Monitor closely
<b>Sibutramine</b>	Increased risk of bleeding – monitor closely
<b>Simvastatin</b>	Generally small clinically irrelevant increase in anticoagulant effects. Monitor initially or after increase in Simvastatin dose
<b>Tamoxifen</b>	Monitor and reduce Warfarin dose as necessary (may require dose reduction of up to half)
<b>Thyroid Hormones</b>	Monitor and adjust Warfarin dose as necessary
<b>Venlafaxine</b>	Anticoagulant effects possibly enhanced – monitor closely

**\*Please note Penicillins and Warfarin:**

Penicillins do not normally alter the effects of Warfarin however a small number of cases of increased prothrombin times and/or bleeding have been reported in patients given Amoxicillin, Ampicillin/Flucloxacillin, Benzylpenicillin, and Co-amoxiclav.

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### **Drugs which reduce anticoagulant effects of Warfarin**

<b>Interacting Drug</b>	<b>Additional Comment</b>
<b>Azathioprine</b>	Monitor as Warfarin dose may need to be increased
<b>Carbamazepine</b>	Warfarin dose may need to be increased – monitor closely. No known interaction with oxcarbazepine
<b>Dexamethasone</b>	May enhance or reduce Warfarin effects -high doses enhance
<b>Oral contraceptives</b>	Generally avoid in thromboembolic disorders
<b>Phenobarbitone</b>	May require 30-60% increase in Warfarin dose. Persists for up to 6 weeks on stopping Phenobarbitone - monitor
<b>Phenytoin</b>	May reduce or enhance anticoagulant effects – monitor closely
<b>Prednisolone</b>	May enhance or reduce Warfarin effects -high doses enhance
<b>Raloxifene</b>	May antagonise Warfarin effect - monitor
<b>Rifabutin</b>	Monitor closely. Reduces anticoagulant effects within 5-7days.
<b>Rifampicin</b>	Warfarin dose may need to be doubled or trebled and reduced on stopping Rifabutin/Rifampicin
<b>Vitamin K</b>	Consider this interaction if patients are Warfarin resistant. Vit K may be present in enteral feeds, health foods, food supplements, green tea.

### **Reporting of drug interactions – Yellow Card**

Prescribers are advised to remain vigilant for the occurrence of drug interactions with all drugs. Particular caution should be exercised when prescribing Warfarin as drug interactions are more common. If you detect an interaction with Warfarin (or any drug) we would strongly encourage you to complete a Yellow Card (back of BNF) or complete a report on the website at [www.yellowcard.gov.uk](http://www.yellowcard.gov.uk)

## **DRUGS TO WATCH WITH WARFARIN**

### **Potential interactions between Warfarin and commonly used herbal and vitamin supplements.**

There is increasing evidence to suggest that interactions do occur between Warfarin and herbal/vitamin supplements. Patients taking Warfarin should avoid herbal and vitamin products unless advised to do so by their doctor and only with appropriate monitoring to allow Warfarin dose adjustments where necessary.

**Please note** **Multivitamin supplements** should be treated with particular caution as they may contain ingredients that affect Warfarin levels. This was highlighted recently by an incident where a patient taking Seven Seas Multibionta 50+® (containing Ginseng and Bilberry) was admitted to hospital with a raised INR.

<b>Product</b>	<b>Potential interaction with Warfarin</b>
<b>Alfalfa</b>	Contains large amounts of Vitamin K – can reduce the anticoagulant effect of Warfarin
<b>Bilberry</b>	May enhance anticoagulant effect – avoid concomitant use
<b>Chamomile</b>	May increase the risk of bleeding
<b>Chondroitin</b>	Chondroitin has anticoagulant activity and should be avoided
<b>Coenzyme Q10</b>	Reduces anticoagulant effect as structurally similar to Vitamin K
<b>Cranberry Juice</b>	Possible enhancement of anticoagulant effect of Warfarin – avoid concomitant use
<b>Devil's claw</b>	May enhance the antiplatelet effects of Warfarin
<b>Dong Quai</b>	Increased risk of bleeding due to inhibition of COX and platelet aggregation. Reports of increases in INR with concurrent use
<b>Evening Primrose Oil</b>	May increase the risk of bruising and bleeding
<b>Fenugreek</b>	May increase the risk of bleeding
<b>Feverfew</b>	May increase bleeding especially in patients already taking certain anti-clotting medications
<b>Flaxseed Oil</b>	May decrease platelet aggregation and increase bleeding
<b>Fish Oils</b>	Fish oils have anti-platelet effects and may increase the risk of bleeding. Monitor closely
<b>Garlic</b>	Increased risk of bleeding due to inhibition of platelet aggregation. Do not take garlic supplements. Regular ingestion of foods containing small amounts of garlic should not pose a problem
<b>Ginger</b>	Large amounts may increase the risk of bleeding – until more is known, monitor INRs closely
<b>Gingko Biloba</b>	Increased risk of bleeding due to inhibition of platelet aggregation and Warfarin metabolism
<b>Ginseng</b>	Increased risk of bleeding due to inhibition of platelet aggregation
<b>Glucosamine</b>	Recent reports of increased INR in patients who had just started Glucosamine. Avoid concomitant use
<b>Grapefruit Juice</b>	May inhibit metabolism and increase Warfarin levels. Avoid or use cautiously

<b>Multivitamin Supplements</b>	Use cautiously in patients taking Warfarin – may contain ingredients that affect Warfarin metabolism eg Ginseng/Bilberry/Vit E
<b>Red Clover</b>	May increase the risk of bleeding
<b>St John's Wort</b>	Reduces anticoagulant effect of Warfarin due to increase in metabolism – avoid concomitant use
<b>Vitamin E</b>	Seems to inhibit platelet aggregation and antagonise the effects of clotting factors. Effects appear to be dose-dependent and are probably clinically significant with 400units/day or more

This table is intended as a quick reference to highlight common interactions between Warfarin and herbal/vitamin supplements. It is not intended to be exhaustive or give detailed information. For further information, prescribers should consult the prescribing support team or resources offering specialised information on drug interactions. Specific queries can also be forwarded by email to Drug Information either at Antrim Hospital ([medicines.info@uh.n-i.nhs.uk](mailto:medicines.info@uh.n-i.nhs.uk)) or the Royal Victoria Hospital ([nirdic@royalhospitals.n-i.nhs.uk](mailto:nirdic@royalhospitals.n-i.nhs.uk))

Useful websites include:

[www.alternativemedicine.com](http://www.alternativemedicine.com)

[www.naturaldatabase.com](http://www.naturaldatabase.com)

[www.medicinescomplete.com](http://www.medicinescomplete.com)

The second and third sites require subscription.