

Interactions with COUMADIN



INDICATIONS

COUMADIN® (warfarin sodium) is a prescription medicine used to treat blood clots and to lower the chance of blood clots forming in your body. Blood clots can cause a stroke, heart attack, or other serious conditions if they form in the legs or lungs. COUMADIN may have been prescribed to help you:

- Reduce your risk of forming blood clots if you have had a heart-valve replacement or if you have an irregular, rapid heartbeat, called atrial fibrillation
- Lower the risk of death if you've had a heart attack, as well as lowering your risk of having another heart attack, stroke, and having blood clots move to another part of your body

It is not known if COUMADIN is safe and effective in children.

IMPORTANT SAFETY INFORMATION

COUMADIN® (warfarin sodium) can cause bleeding which can be serious and sometimes lead to death.

You may have a higher risk of bleeding if you take COUMADIN and:

- are 65 years old or older
- have a history of stomach or intestinal bleeding
- have high blood pressure (hypertension)
- have a history of stroke, or "mini-stroke" (transient ischemic attack or TIA)
- have serious heart disease
- have a low blood count or cancer
- have had trauma, such as an accident or surgery

- have kidney problems
- take other medicines that increase your risk of bleeding, including:
 - a medicine that contains heparin
 - other medicines to prevent or treat blood clots
 - non-steroidal anti-inflammatory drugs (NSAIDs)
- take warfarin sodium for a long time. Warfarin sodium is the active ingredient in COUMADIN.

Call your doctor or seek immediate medical care if you have any of the following signs or symptoms of bleeding:

- pain, swelling, or discomfort
- headaches, dizziness, or weakness
- unusual bruising (bruises that develop without known cause or grow in size)
- nosebleeds or bleeding gums
- bleeding from cuts takes a long time to stop
- menstrual bleeding or vaginal bleeding that is heavier than normal
- pink or brown urine; red or black stools
- coughing up or vomiting blood; or vomiting material that looks like coffee grounds

Please see additional Important Safety Information on page 2 and [full Prescribing Information](#), including **Boxed WARNING regarding bleeding risk.**

COUMADIN®
(Warfarin Sodium Tablets, USP) Crystalline

1 mg 2 mg 2.5 mg 3 mg 4 mg 5 mg 6 mg 7.5 mg 10 mg



IMPORTANT SAFETY INFORMATION (continued)

Do not take COUMADIN® (warfarin sodium) if:

- **your chance of having bleeding problems is higher than the possible benefit of treatment.** Your healthcare provider will decide if COUMADIN is right for you. Talk to your healthcare provider about all of your health conditions
- **you are pregnant.** COUMADIN may cause birth defects, miscarriage, or death of your unborn baby. If you are **pregnant and have a mechanical heart valve**, talk to your doctor about whether the benefit of taking COUMADIN outweighs the risks
- **you are allergic to warfarin or any of the other ingredients in COUMADIN**

It is important to tell your healthcare provider about all prescription and non-prescription medicines, vitamins, and herbal supplements you take. Some of your medicines may affect the way COUMADIN works and affect the dose of COUMADIN you need or increase COUMADIN side effects.

- **Do not change or stop any of your medicines or start any new medicines, vitamins, and herbal supplements without talking to your healthcare provider**
- **Do not take other medicines that contain warfarin sodium while taking COUMADIN.**
- **Get your regular blood test (INR) to check for your response to COUMADIN.** The INR test checks to see how fast your blood clots. Your healthcare provider will decide what INR numbers are best for you and adjust your dose of COUMADIN to keep your INR in a target range.

Some foods and beverages can interact with COUMADIN and affect your treatment and dose.

- Eat a normal, balanced diet and talk to your healthcare provider before making any diet changes. Do not eat large amounts of leafy green vegetables, which contain vitamin K. Certain vegetable oils also contain large amounts of vitamin K. Too much vitamin K can lower the effect of COUMADIN

Before taking COUMADIN, tell your healthcare provider if you:

- have bleeding problems, fall often, have liver or kidney problems, have high blood pressure, have a heart problem called congestive heart failure, have diabetes, or have any other medical conditions.

- **are planning to have any surgery or dental procedure** because you may have to stop taking COUMADIN for a short time or your dose may need to be adjusted.
- **are pregnant or plan to become pregnant or considering breast-feeding** while taking COUMADIN

Other possible serious side effects of COUMADIN include:

- **Death of skin tissue (skin necrosis or gangrene).** This can happen soon after starting COUMADIN. It happens because blood clots form and block blood flow to an area of your body. Call your healthcare provider right away if you have pain, color, or temperature change to any area of your body. You may need medical care right away to prevent death or loss (amputation) of your affected body part
- **“Purple toes syndrome.”** Call your healthcare provider right away if you have pain in your toes and they look purple or dark in color.

Take COUMADIN exactly as prescribed by your doctor.

- Don't stop taking COUMADIN without talking to your doctor as your risk of stroke may increase
- Call your healthcare provider right away if you take too much COUMADIN, are sick with diarrhea, an infection, or have a fever, or fall or injure yourself, especially if you hit your head.

DRUG INTERACTIONS

It is important that the level of COUMADIN in your body remains consistent. There are many products, including prescription drugs, over the counter drugs, herbal products, foods and other substances that can change the level of COUMADIN in your body due to how these products are metabolized or broken down.

It is important to understand how these interactions may affect the levels of COUMADIN in your body. You will need to have your INR monitored more frequently when starting or stopping other drugs, including herbal products, or when changing dosages of other drugs, including drugs intended for short-term use such as antibiotics. It is also important to read the labels of all products to determine any possible interactions with COUMADIN and adverse events related to bleeding. Be sure to tell your doctor of all medications and substances you take while on COUMADIN therapy.

Interactions with COUMADIN® (Warfarin Sodium Tablets, USP) Crystalline

You should also tell all your healthcare providers that you are taking COUMADIN® (warfarin sodium), as this may affect your treatments for other medical conditions.

A blood test called an INR or International Normalized Ratio measures how fast your blood clots and compares it to an average. The higher the INR, the longer it takes blood to clot. INR tests are important in helping your doctor determine your response to COUMADIN.

CYP450 Interactions

CYP is a gene family and is also commonly known as the Cytochrome P450 or CYP450 gene family. A gene family is a group of genes that share important characteristics.

There are certain enzymes that are produced by the Cytochrome P450 genes that play a role in the metabolism or breakdown of some medications and substances in your body, including COUMADIN.

Certain products, known as inhibitors of the CYP450 enzymes, may increase the effect of COUMADIN and increase your INR

- Increasing the effect of COUMADIN may increase your risk of bleeding

Certain products, known as inducers of the CYP450 enzymes, may decrease the effect of COUMADIN and decrease your INR

- Decreasing the effect of COUMADIN may put you at risk for forming blood clots

The table below lists examples of medications and products that can inhibit or induce the effect of COUMADIN. **Please note that this list is not all-inclusive.** It is important to note that certain medications and products can act as inhibitors and also inducers of CYP450 depending upon the specific enzyme interactions.

Make sure to tell all your healthcare providers about any medications or other products taken while on COUMADIN therapy.

Examples of CYP450* Interactions with COUMADIN

INHIBITORS

(May **increase** the effect of COUMADIN and your INR)

Acyclovir - Zovirax®

Allopurinol - Alloprim®, Zyloprim®

Alprazolam - Niravam®, Xanax®, Xanax® XR

Amiodarone - Cordarone®, Nexterone®, Pacerone®

Amlodipine -

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|----------------|--------------|
| - Amturnide® | - Lotrel® |
| - Azor® | - Norvasc® |
| - Caduet® | - Tekamlo® |
| - Exforge® | - Tribenzor® |
| - Exforge® Hct | - Twynsta® |

Aprepitant - Emend®

Atorvastatin - Caduet®, Lipitor®

Atazanavir - Reyataz®

Bicalutamide - Casodex®

Caffeine

Capecitabine - Xeloda®

Cilostazol - Pletal®

Cimetidine - Tagamet®, Tagamet® HB

Ciprofloxacin - Cipro®, Cipro® XR

Clarithromycin - Biaxin®, Biaxin® XL, Prevpac®

Conivaptan - Vaprisol®

Co-Trimoxazole - Bactrim®, Septra®

Cyclosporine - Gengraf®, Neoral®, Sandimmune®

Darunavir/Ritonavir - Kaletra®, Norvir®, Prezista®

Diltiazem -

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|----------------|--------------|
| - Cardizem® | - Dilt®- CD |
| - Cardizem® CD | - Diltzac® |
| - Cardizem® LA | - Taztia® XT |
| - Cartia® XT | - Tiazac® |
| - Dilacor® XR | |

Disulfiram - Antabuse®

Erythromycin -

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|------------|---------------|
| - E.E.S® | - Erythrocin® |
| - Ery-Tab® | - PCE® |
| - Eryc® | |

Etravirine - Intelence®

Famotidine -

- | | |
|-----------|--------------------|
| - Duexis® | - Pepcid® AC |
| - Pepcid® | - Pepcid® Complete |

Interactions with COUMADIN® (Warfarin Sodium Tablets, USP) Crystalline

Examples of CYP450*

Interactions with COUMADIN® (warfarin sodium)

(Continued)

INHIBITORS

(May **increase** the effect of COUMADIN and your INR)

Fluconazole - Diflucan®

Fluoxetine -

- Prozac®
- Prozac® Weekly
- Sarafem®
- Symbyax®

Fluvastatin - Lescol®, Lescol® XL

Fluvoxamine - Luvox®, Luvox® XR

Fosamprenavir - Lexiva®

Imatinib - Gleevec®

Indinavir - Crixivan®

Isoniazid -

- Isoniazid®
- Isonarif®
- Rifamate®
- Rifater®

Itraconazole - Onmel®, Sporanox®

Ketoconazole - Nizoral®

Lopinavir/Ritonavir - Kaletra®

Methoxsalen - 8-Mop®, OxSORalen®-Ultra, Uvadex®

Metronidazole -

- Flagyl®
- Flagyl® ER
- Helidac®
- Pylera®

Mexiletine Hydrochloride

Miconazole - Oravig®

Nefazodone Hydrochloride

Nelfinavir - Viracept®

Nilotinib - Tasigna®

Norfloxacin - Noroxin®

Oral Contraceptives

Oxandrolone - Oxandrin®

Phenylpropanolamine

Posaconazole - Noxafil®

Propafenone - Rythmol®, Rythmol® SR

Propranolol -

- Inderal®
- Inderal® LA
- Inderide®
- Innopran® XL

Ranitidine - Zantac®

Ranolazine - Ranexa®

Ritonavir - Kaletra®, Norvir®

Saquinavir - Invirase®

INHIBITORS

(May **increase** the effect of COUMADIN and your INR)

Telithromycin - Ketek®

Terbinafine - Lamisil®

Ticlopidine Hydrochloride

Tigecycline - Tygacil®

Tipranavir - Aptivus®

Verapamil -

- Calan®
- Calan® SR
- Covera®-HS
- Tarka®
- Verelan®
- Verelan® PM

Voriconazole - Vfend®

Zafirlukast - Accolate®

Zileuton - Zylflo®, Zylflo® CR

Please note that this list is not all-inclusive. Make sure to tell all your healthcare providers, including your pharmacist, about any medications or other products taken while on COUMADIN therapy.

INDUCERS

(May **decrease** the effect of COUMADIN and your INR)

Aprepitant - Emend®

Armodafinil - Nuvigil®

Bosentan - Tracleer®

Carbamazepine -

- Carbatrol®
- Epitol®
- Equetro®
- Tegretol®
- Tegretol®- XR
- Teril®

Cigarette Smoking

Efavirenz - Atripla®, Sustiva®

Etravirine - Intelence®

Modafinil - Provigil®

Montelukast - Singulair®

Nafcillin - Nallpen® In Plastic Container

Omeprazole -

- Nexium®
- Prilosec®
- Prilosec® OTC
- Zegerid®
- Zegerid® OTC

Phenobarbital - Donnatal®

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Please see Indications and Important Safety Information on pages 1-2 and [full Prescribing Information](#), including **Boxed WARNING** regarding bleeding risk.

Interactions with COUMADIN® (Warfarin Sodium Tablets, USP) Crystalline

Examples of CYP450*

Interactions with COUMADIN® (warfarin sodium) (Continued)

INDUCERS

(May **decrease** the effect of COUMADIN and your INR)

Phenytoin - Dilantin®, Phenytek®

Pioglitazone -

- Actoplus® Met
- Actoplus® Met XR
- Actos®
- Duetact®
- Oseni®

Prednisone - Rayos®

Rifampin -

- Rifadin®
- Rifamate®
- Rifater®
- Rimactane®

Rufinamide - Banzel®

Please note that this list is not all-inclusive. Make sure to tell all your healthcare providers, including your pharmacist, about any medications or other products taken while on COUMADIN therapy.

Drugs that Increase Bleeding Risk

There are also drugs that can increase your risk of bleeding. When these drugs are given together with COUMADIN the risk of bleeding increases and your INR levels will need to be more closely monitored.

Drugs* that Increase the Risk of Bleeding

| DRUG CLASS | EXAMPLES OF SPECIFIC DRUGS |
|------------|----------------------------|
|------------|----------------------------|

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|----------------|---|
| Anticoagulants | <ul style="list-style-type: none"> - argatroban - Acova® - dabigatran - Pradaxa® - bivalirudin - Angiomax® - desirudin - Iprivask® - heparin sodium - lepirudin - Refludan® |
|----------------|---|

| | |
|---------------------|---|
| Antiplatelet Agents | <ul style="list-style-type: none"> - aspirin - cilostazol - Pletal® - clopidogrel - Plavix® - dipyridamole <ul style="list-style-type: none"> - Aggrenox® - Persantine® - prasugrel - Effient® - ticlopidine |
|---------------------|---|

Drugs* that Increase the Risk of Bleeding (Continued)

| DRUG CLASS | EXAMPLES OF SPECIFIC DRUGS |
|------------|----------------------------|
|------------|----------------------------|

| | |
|---------------------------------------|---|
| Nonsteroidal Anti-inflammatory Agents | <ul style="list-style-type: none"> - celecoxib - Celebrex® - diclofenac <ul style="list-style-type: none"> - Arthrotec® - Cambia® - Cataflam®, - Voltaren®-XR - Zipsor® - diflunisal - fenoprofen - Nalfon® - ibuprofen <ul style="list-style-type: none"> - Advil® - Midol® Liquid Gels - Motrin® - Profen® - Tab-Profen® - indomethacin - Indocin® - ketoprofen - Nexcede® - ketorolac - Sprix® - mefenamic acid <ul style="list-style-type: none"> - Ponstel® - Treximet® - Vimovo® - naproxen <ul style="list-style-type: none"> - Aleve® - Anaprox® - Anaprox® DS - EC-Naprosyn® - Naprelan® - Naprosyn® - oxaprozin - Daypro® - piroxicam - Feldene® - sulindac - Clinoril® |
|---------------------------------------|---|

Please note this is not an all-inclusive list. Make sure to tell all your healthcare providers, including your pharmacist, about any medications or other products taken while on COUMADIN therapy.
* The brands listed (other than COUMADIN) are registered trademarks of their respective owners and are not trademarks of Bristol-Myers Squibb Company

Please see Indications and Important Safety Information on pages 1-2 and [full Prescribing Information](#), including **Boxed WARNING** regarding bleeding risk.

Drugs* that Increase the Risk of Bleeding (Continued)

| DRUG CLASS | EXAMPLES OF SPECIFIC DRUGS | |
|-------------------------------|-----------------------------------|-----------|
| Serotonin Reuptake Inhibitors | - citalopram - Celexa® | |
| | - desvenlafaxine - Pristiq® | |
| | - duloxetine - Cymbalta® | |
| | - escitalopram - Lexapro® | |
| | - fluoxetine | - Prozac® |
| | - Prozac® Weekly | |
| | - Sarafem® | |
| | - Symbyax® | |
| | - fluvoxamine - Luvox®, Luvox® XR | |
| | - milnacipran - Savella® | |
| | - paroxetine | - Paxil® |
| | - Paxil® CR | |
| | - Pexeva® | |
| | - sertraline - Zoloft® | |
| | - venlafaxine - Effexor® XR | |
| - vilazodone - Viibryd® | | |

Please note this is not an all-inclusive list. Make sure to tell all your healthcare providers, including your pharmacist, about any medications or other products taken while on COUMADIN® (warfarin sodium) therapy.

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Antibiotics and Antifungals

In addition to the possible CYP450 interactions seen with using COUMADIN with certain antibiotics or antifungals mentioned earlier, there have been reports of changes in the INR in patients taking COUMADIN with antibiotics or antifungals. Clinical studies have not shown consistent effects of antibiotics or antifungals on the levels of COUMADIN in the blood.

If you are starting a new medication, even for a short period of time, such as an antibiotic, it is important to be aware of possible interactions. You may need to have your INR measured more frequently.

Herbal Products and Foods

Many different common herbal products and foods can interact with COUMADIN and change the way COUMADIN works in your body. Herbal products have several common and scientific names and their potency (or strength) may vary from one brand to another. These products and their variations may affect the potential interaction with COUMADIN.

Some herbal products, such as garlic and Ginkgo biloba, may cause bleeding when taken alone and may also increase the effect of COUMADIN.

- Increasing the effect of COUMADIN may increase your risk of bleeding

Some herbal products, such as co-enzyme Q10, St. John's wort, and ginseng, may decrease the effect of COUMADIN.

- Decreasing the effect of COUMADIN may put you at risk for forming blood clots

Some herbal products and foods can interact with COUMADIN through CYP450 interactions, including:

- Echinacea
- Grapefruit juice
- Ginkgo
- Goldenseal
- St. John's wort

It is important to talk to your doctor about any herbal products you are taking.

Additional INR monitoring may be required for any herbal products that you start or stop taking.

Make sure to tell your healthcare provider about any medications or other substances ingested while on COUMADIN therapy. You can use the My Meds Wallet Card to record all your medications, herbal products and other substances to help prepare you for your conversation with your healthcare provider.

For additional information and tools to help you understand and manage your COUMADIN therapy with your doctor, visit www.coumadin.com



Make sure to tell your healthcare provider about any medications or other substances ingested while on COUMADIN® (warfarin sodium) therapy.

You can use the My Meds Wallet Card below to record all your medications, herbal products and other substances to help prepare you for your conversation with your healthcare provider. If there are changes to what you list on your card, you can go to www.coumadin.com and select the Medications and COUMADIN tab to print a new card and update your information.

For additional information and tools to help you understand and manage your COUMADIN therapy with your doctor, visit www.coumadin.com

MY MEDICATIONS

| MEDICATIONS/HERBAL SUPPLEMENTS | DAILY DOSE |
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You can fold this card in half to fit neatly in your wallet.

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