

Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

Coumadin 1 mg tablets

Active ingredient and its quantity:

Each tablet contains:

warfarin sodium 1 mg

Coumadin 2 mg tablets

Active ingredient and its quantity:

Each tablet contains:

warfarin sodium 2 mg

Coumadin 2.5 mg tablets

Active ingredient and its quantity:

Each tablet contains:

warfarin sodium 2.5 mg

Coumadin 5 mg tablets

Active ingredient and its quantity:

Each tablet contains:

warfarin sodium 5 mg

Inactive ingredients and allergens: see section 2 under 'Important information about some of this medicine's ingredients' and section 6, 'Additional information'.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

1. What is this medicine intended for?

Prophylaxis and treatment of thrombosis.

Therapeutic group: Anticoagulants, vitamin K antagonists.

2. Before using this medicine

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredient (warfarin sodium) or to any of the other ingredients in this medicine (listed in section 6).
- You are pregnant, may become pregnant or gave birth within the last 48 hours.
- You have or have ever had any bleeding problems.
- You recently had a stroke caused by bleeding in the brain.
- You had surgery within the last 72 hours or are going to have surgery within the next 72 hours.
- You are taking non-steroidal anti-inflammatory drugs (NSAIDs), aspirin or anticoagulants, since using them in combination with Coumadin may increase the risk of bleeding (see section 'Drug interactions').

If any of these conditions applies to you, do not take this medicine and go back to your doctor to discuss your treatment.

Special warnings about using this medicine

Before treatment with Coumadin, tell your doctor if:

- you have very high blood pressure that is not controlled by medicines.
- you have or have ever had a stomach or duodenal ulcer.
- you previously had gastrointestinal bleeding.

- you recently had an ischemic stroke (caused by blockage of blood vessels in the brain).
- you have a bacterial infection of the heart lining (endocarditis).
- you have problems with blood circulation to the brain (cerebrovascular disease).
- you have thyroid problems.
- you have severe heart disease, liver or kidney problems.
- you have a condition making you prone to blood clots (thrombophilia).
- you have anemia (low hemoglobin level causing extreme tiredness, breathlessness and poor resistance to infections).
- you have a tumor or cancer.
- you were recently bruised or injured.
- you are at a higher risk of bleeding, for example, if you are over 65 years old or are unsteady on your feet and more likely to fall and injure yourself.

If any of these conditions apply to you, tell your doctor or pharmacist before taking Coumadin, because you may need to be checked more often during treatment. Always tell your doctor, surgeon, nurse, dentist or pharmacist that you are taking Coumadin (warfarin).

Factors which affect Coumadin:

A number of factors affect blood clotting, and therefore affect Coumadin treatment. To make sure that Coumadin works properly and safely, it is important to follow the advice below.

Increases the effect of Coumadin	Reduces the effect of Coumadin	What to do
Weight loss	Weight gain	Do not start a weight reducing diet or change your eating habits without discussing it first with your doctor or nurse. Keep your level of activity as close to normal as possible.
	Vitamin K	Vitamin K supplements should be taken only if prescribed by doctors, as sudden increase in vitamin K intake may decrease the effect of Coumadin.
	Foods such as liver, broccoli, Brussels sprouts and green leafy vegetables contain large amounts of vitamin K.	Don't make any major changes in your diet while taking Coumadin.
Cranberry juice and cranberry products (and possibly grapefruit juice)		Don't drink either cranberry juice or grapefruit juice or consume products containing cranberries and grapefruit while taking Coumadin.
Large amounts of alcohol		Only drink small amounts while taking Coumadin.

Increases the effect of Coumadin	Reduces the effect of Coumadin	What to do
Sudden illness such as the flu or feeling exhausted	Stomach upset, diarrhea, vomiting	If any of these happen, tell your doctor or nurse, as your dose may need to be changed.
Stopping smoking		Seek medical advice before you stop smoking

Surgery

Due to the risk of bleeding, you may need to have your dosage lowered before surgery or a tooth extraction. Stop taking Coumadin (warfarin) 72 hours before and after surgery when there is a risk of severe bleeding. Tell your doctor or dentist that you are taking warfarin.

Smoking

Consult your doctor if you decide to give up smoking because giving up smoking may increase the effect of the medicine.

Tests and follow-up

During the course of treatment with this medicine, you will need to have regular tests for blood coagulation. These blood tests are very important in order to make sure that you are taking the correct dosage. You will have these blood tests more frequently if your dosage is changed, if you start or stop using other medicines, or if you have liver or kidney problems.

Drug interactions

If you are taking or have recently taken any other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist.

Do not take this medicine, and tell your doctor if you are taking the following medicines:

- alteplase, reteplase, streptokinase, tenecteplase, urokinase (fibrinolytic medicines for treating or preventing blood clots);
- St. John's Wort (*hypericum perforatum*) - a herbal remedy for depression.

Tell your doctor before you start taking the following medicines:

- non-steroidal anti-inflammatory drugs (NSAIDs) for pain and inflammation, including aspirin, ibuprofen, celecoxib, diclofenac, indomethacin, meloxicam;
- clopidogrel, abciximab, dipyridamole, eptifibatide, tirofiban (antiplatelet medicines to prevent or breakdown blood clots);
- heparin or medicines containing heparin, bivalirudin, fondaparinux, dabigatran, rivaroxaban, danaparoid, prostacyclin (other anticoagulants);
- sulfinpyrazone (for treatment of gout);
- glucosamine (for treatment of osteoarthritis);
- SSRI and SNRI anti-depressants such as citalopram, fluoxetine, paroxetine, venlafaxine;
- some types of medicines used to prevent blood clotting (such as warfarin, dicoumarol, phenprocoumon, acenocoumarol and fluindione). The effect of these medicines may be stronger when taken with glucosamine. Patients who take such combinations should be monitored with special care when initiating or ending glucosamine therapy.

Medicines that increase the effect of this medicine. Tell your doctor if you are taking:

- prolonged, regular use of paracetamol (for pain or inflammation);
- antibiotics, such as amoxicillin, levofloxacin, and tetracycline;
- allopurinol (for gout);
- capecitabine, erlotinib, tamoxifen (for types of cancer);

- disulfiram (for alcohol dependence);
- ketoconazole, fluconazole, itraconazole (for fungal infections);
- omeprazole (for stomach ulcers);
- propafenone, amiodarone, quinidine (for heart disorders);
- methylphenidate (for attention deficit disorders);
- zafirlukast (for asthma);
- bezafibrate, ciprofibrate, fenofibrate, gemfibrozil (to reduce blood fats);
- statins such as fluvastatin to lower cholesterol (not including pravastatin);
- erythromycin, sulfamethoxazole, metronidazole (for bacterial infections);
- orlistat (for obesity).

Medicines that reduce the effect of this medicine. Tell your doctor if you are taking:

- barbiturates (sedatives);
- primidone, phenytoin, carbamazepine (to treat epilepsy);
- griseofulvin (for fungal infections);
- oral contraceptives;
- rifampicin (for tuberculosis);
- azathioprine (for inflammatory bowel disease and rheumatoid arthritis and to prevent transplanted organ rejection);
- sucralfate (for stomach ulcers);
- cholestyramine (for lowering cholesterol);
- vitamin K (increased consumption of vitamin K may reduce the effect of warfarin).

Medicines that have varying effects on this medicine. Tell your doctor if you are taking:

- corticosteroids (for inflammations and many other diseases);
- nevirapine, ritonavir (for HIV infection).

Using this medicine and food

Seek medical advice before you make any major changes in your diet while taking Coumadin tablets. Refrain from cranberry products. Certain other foods may affect how well Coumadin treatment works. See details at the beginning of section 2 under "Factors which affect Coumadin".

Using this medicine and alcohol consumption

Acute consumption of a large amount of alcohol may inhibit the metabolism of warfarin and increase INR. Conversely, chronic heavy alcohol intake may increase the metabolism of warfarin. See details at the beginning of section 2 under "Factors which affect Coumadin".

Pregnancy, breastfeeding and fertility

Do not use this medicine if you are pregnant, may become pregnant or gave birth within the last 48 hours. Consult your doctor immediately if you get pregnant while using this medicine. If you are breastfeeding, it is unlikely that the medicine will harm your baby as long as you are taking the correct dosage.

Driving and using machines

This medicine has no known effect on the ability to drive or to operate machines.

Important information about some of this medicine's ingredients

This medicine contains lactose (a type of sugar). If you have been told that you have an intolerance to certain sugars, tell your doctor before you start using this medicine. Each tablet contains less than 1 mmol (23 mg) sodium, that is to say essentially 'sodium-free'.

3. How to use this medicine?

Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine.

Only your doctor will determine your dose and how you should take this medicine.

Your dosage depends on the results of the blood tests carried out to measure the time it takes for your blood to clot. Be sure to take the dose at the same time every day.

Do not exceed the recommended dose.

Do not chew! Swallow the medicine with water. Do not keep the medicine in your mouth longer than the time it takes to swallow it. If your prescribed dose is half a tablet, split the tablet using a tablet-splitting device.

If you have taken an overdose or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you. Symptoms of overdose include bleeding, black tarry stools, blood in urine, heavy or continuous bleeding from cuts or wounds or unusually heavy menstrual bleeding.

If you forget to take this medicine

If you usually take this medicine in the evening and you forget to take the medicine, if you remember before midnight on the same day, take the forgotten dose. If midnight has passed, do not take the forgotten dose. Take your normal dose the next day at the usual time.

If you usually take this medicine in the morning and you forget to take it, take the medicine as soon as you remember and continue with the regular schedule.

But if it is already time to take your next dose, do not take the forgotten dose. Never take a double dose to compensate for a forgotten one!

Make a note for yourself that you missed a dose. If you are not sure what to do if you forgot a dose, ask your doctor.

Adhere to the treatment as recommended by your doctor. Even if your health improves, do not stop taking this medicine without consulting your doctor or pharmacist.

Do not take medicines in the dark! Check the label and dose every time you take medicine. Wear glasses if you need them.

If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. Side effects

Like with all medicines, using Coumadin may cause side effects in some users. Do not be alarmed by this list of side effects. You may not experience any of them.

Stop using this medicine and go to the hospital immediately if:

- You experience a rare allergic reaction, such as swelling of the face, tongue, lips and throat, difficulty breathing, severe itching of your skin with raised lumps. You may need urgent medical attention.
- You fell or injured yourself during treatment, especially if you hit your head. Seek urgent medical care. You may need a doctor's examination since you will be at increased risk of bleeding.

Consult your doctor immediately if the following appear (the frequency of these effects is not known):

- unexpected bleeding or signs of bleeding (this could mean that your clotting values are too low and that your dosage needs to be adjusted);
- unexplained nose bleeds or bleeding of the gums;
- bruising or red spots on your skin for no apparent reason;
- heavy or continuous bleeding from wounds and cuts;
- pink, dark red or brown urine (this may be due to bleeding in the bladder or kidneys);

- black tarry stools, vomiting of blood or particles that look like coffee grounds (signs of bleeding in the stomach or intestines), bleeding from the rectum;
- coughing up blood;
- (in women) unusually heavy menstrual bleeding or bleeding from the vagina;
- blurred vision, slurred speech, loss of movement, numbness, dizziness, headache, nausea or vomiting, spasms, loss of consciousness, which may be signs of bleeding in the brain;
- painful, blue-purple colored toes;
- yellowing of the skin and white of the eye (jaundice), liver problems;
- severe pain in the upper abdomen (a sign of inflammation of the pancreas);
- difficulties breathing and chest pain due to collection of blood in the chest;
- painful skin rash. In rare cases, warfarin may cause serious skin effects, including an effect known as calciphylaxis, which can start as a painful skin rash, but may lead to other serious complications. This side effect occurs more frequently in patients with chronic kidney disease;
- impairment of renal function occurring with excessive anticoagulation and presence of blood in urine (anticoagulant-related nephropathy).

If any of the following side effects persists, gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor or pharmacist:

nausea or vomiting, diarrhea, hair loss, skin rash, fever, sharp drop in the number of red blood cells or in the blood hemoglobin level (shown in blood tests).

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il), which links to an online form for reporting side effects. You can also use this link: <https://sideeffects.health.gov.il>

5. How to store the medicine?

Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor!

Do not use the medicine after the expiry date (exp. date) stated on the package. The expiry date refers to the last day of that month.

Storage conditions: Store below 25°C.

Do not throw away medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines that you no longer use. These measures will help protect the environment.

6. Additional information

In addition to the active ingredient, this medicine also contains:

Lactose anhydrous, pregelatinized starch, magnesium stearate, color lakes (**1 mg:** D&C Red No.6 barium lake, **2 mg:** FD&C Blue No.2 lake, FD&C Red No.40 lake, **2.5 mg:** FD&C Blue No.2 lake, D&C Yellow No.10 lake, **5 mg:** D&C Yellow No.10 lake, D&C Red No.6 barium lake)

What the medicine looks like and contents of the pack:

Plastic bottle with a child-proof cap. Each package contains 30/100/1,000 tablets.

Not all pack sizes may be marketed.

Tablet appearance:

Coumadin 1 mg – flat, pink, capsule-shaped tablet, debossed with WARFARIN TARO on one side and a score line and the numeral “1” on the other side.

Coumadin 2 mg – flat, lavender, capsule-shaped tablet, debossed with WARFARIN TARO on one side and a score line and the numeral “2” on the other side.

Coumadin 2.5 mg – flat, green, capsule-shaped tablet, debossed with WARFARIN TARO on one side and a score line and the number “2½” on the other side.

Coumadin 5 mg – flat, peach, capsule-shaped tablet, debossed with WARFARIN TARO on one side and a score line and the numeral “5” on the other side.

Name and address of the manufacturer and registration-holder:

Taro Pharmaceutical Industries Ltd., 14 Hakitor St., Haifa Bay 2624761

Registration number of the medicine in the Ministry of Health National Drug Registry:

Coumadin 1 mg tablets: 111-43-29373-00

Coumadin 2 mg tablets: 111-44-29374-00

Coumadin 2.5 mg tablets: 111-45-29375-00

Coumadin 5 mg tablets: 111-48-29378-00

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