

Warfarin- All you need to know

Warfarin is an oral anticoagulant. Its role is to prevent blood clots. Its main use is to prevent clots with atrial fibrillation (a type of irregular heart beat that can lead to blood clots), artificial heart valves, deep vein thrombosis, pulmonary embolism (blood clot in the lungs) and strokes. Warfarin is sometimes used after myocardial infarction (after heart attack) however warfarin is not as effective as antiplatelet drugs at preventing or treating clots in coronary arteries. Hence antiplatelet drugs such as clopidogrel (Plavix[®], Clodel[®]) or aspirin are more often used after myocardial infarction. Nearly 40,000 people in Ireland use warfarin¹ and this number is likely to rise in the coming years as our population gets older and with better screening techniques.²

How it works?

Warfarin is described as a blood thinner however this is not an accurate description. Warfarin does not actually thin the blood or make it less viscous. The blood needs vitamin K to be able to clot. Warfarin acts by reducing the production of vitamin K in the liver. It works indirectly so has no effect on clots already formed. It is used to prevent rather than treat clots. Therefore it is ineffective in treating myocardial infarction and strokes as the clots have already formed. It takes about 24 hours to exert its effect and has a half life of 36 hours. Its peak effect can take up to 3 days and may last up to 5 days.

Contraindications

Warfarin should not be used for pregnancy (can cause foetal haemorrhage, particularly in the first and third trimesters), severe hypertension, renal (kidney) impairment (avoid if creatinine clearance is less than 10ml/minute) and in patients with peptic ulcers.³

Checking Warfarin level

The dose of warfarin you should be taking is determined by measurement of the International Normalised Ratio (INR). This is a ratio of the patient's prothrombin time to an international standard. Put simply, this test measures the clotting tendency of blood as compared to an international standard. Many factors influence how the body responds to warfarin, therefore INR needs to be checked regularly. The INR is normally checked at least once a month but more frequent checking may be needed depending on the patient's condition and factors such as diet, other medication etc. The INR level required varies depending on the condition, but a level of between 2 and 3 is normally required. The risk of bleeding increases greatly with an INR of above 5.

The optimal INR is uncertain, but there are some general guidelines depending on the condition warfarin is being used for. An INR of between 2 and 2.5 is recommended for prevention of deep vein thrombosis including surgery in high risk patients while a level of between 2 and 3 is recommended for hip surgery and fractured femur operations. An INR between 2 and 3 is recommended for atrial fibrillation, artificial heart valves made from tissue (usually using a valve of an animal like a pig)*, deep vein thrombosis, pulmonary embolism, transient ischaemic attacks (mini strokes) and strokes. An INR of between 3 and 4.5 is needed in some situations because of increased risk of clot. This includes recurrent deep vein thrombosis and pulmonary embolism, arterial disease including myocardial infarction and mechanical prosthetic heart valves*.

*An artificial valve is a device implanted into the heart when a patient's heart valves are damaged, known as heart valve disease. There are many causes of heart valve damage including high blood pressure and myocardial infarction.

Heart valve disease disrupts the flow of blood through the heart and leads to symptoms like shortness of breath and weakness. There are two types of artificial valves used to substitute damaged valves, a mechanical valve which is made from metal or a tissue valve which is when the valve of an animal (eg. pig) is inserted. The mechanical valve has the advantage that it can last indefinitely however it damages red blood cells which can lead to clots, hence the need for long term warfarin. The tissue valve has the advantage that there is less risk of clot, which means that patients often do not need to take warfarin after getting one inserted. However, the major disadvantage of a tissue valve is that it doesn't last as long as mechanical valves, often needing to be replaced after 15 years.

How often should INR be checked?

INR should be checked daily or on alternate days after starting warfarin. After the patient leaves hospital; weekly INR checks are recommended for 4 to 6 weeks. After this, INR checks can be extended to once every 8 weeks if the patient is showing good control.⁴ Changes in the patient's medical condition such as heart disease, liver disease, thyroid status or change in drug therapy may alter anticoagulant control and will mean more frequent INR checks are needed.⁵

Dose of warfarin

The usual starting dose is 10mg for 2 days.⁶ A prothrombin time should be measured prior to commencement of warfarin to assess liver function. The dose should be taken at the same time each day, usually between 5-7 pm, and the INR measured 16 hours later, i.e. between 9 and 11am the next morning.⁷ The starting dose should be lower in the following situations: prolonged prothrombin time, abnormal liver function tests, congestive heart failure, parental feeding (intravenous feeding when the patient can not eat), underweight patients (BMI less than 18), medication that increase the affect of warfarin and in the elderly (over 80 years).

For most patients, the daily dose of warfarin tends to fall between 3mg and 9mg. However responses can vary widely between patients and in the same patient over a period of treatment. Rarely a patient may have a hereditary resistance to warfarin and require large doses of warfarin or may respond more effectively to a different type of oral anticoagulant.⁸ In the UK and Ireland, warfarin tablets come in three strengths and each has a universally agreed colour to distinguish strengths. Warfarin 1mg are a brown colour, warfarin 3mg are a blue colour and warfarin 5mg are a red colour.

Precautions

Warfarin should be taken at the same time each day. This ensures accuracy of INR results. A missed dose must be recorded. A missed dose should be taken within 12 hours and the normal dosing schedule resumed the next day. Never double up the next day if you miss a day. Over the counter (OTC) drugs should be used in caution. Aspirin and NSAIDs (ibuprofen) should be avoided as they increase risk of bleeding. Paracetamol is safe to take as a painkiller while taking warfarin. Significant changes in intake of food high in Vitamin K (e.g. liver, green leafy vegetables) affects the action of warfarin and more frequent monitoring may be required. Alcohol consumption below 2 units per day (one drink per day) has no effect on the INR but going above this level can affect INR. Weight reducing diets can affect INR level so it must be monitored more closely if you are losing weight. Avoid drinking cranberry juice as it can affect warfarin levels.

Bleeding is the most common side effect of warfarin. It more often occurs in the first month of treatment and is more common in patients over 65.⁹ Signs of bleeding to watch out for include excessive bruising, bleeding gums, nose bleeds, blood in urine, blood in stools (can be characterised by red or black stools), coughing up blood, excessively heavy periods and severe headaches. Patients must get immediate medical attention if they are unable to stop bleeding, are involved in an accident or get a significant blow to the head. If you have a nose bleed while taking warfarin, lean your head forward and pinch below the bridge of your nose firmly for ten minutes. If a nose bleed lasts for more than 15 minutes or you are having regular nose bleeds, you should get immediate medical attention. Patients should carry anticoagulant booklets for the recording of INR results and anticoagulation dose. These are available from the warfarin clinic or your doctor's surgery. Contact sport like Gaelic football or rugby are best avoided when taking warfarin. Use a soft tooth brush to avoid bleeding of the gums. Take extra care when shaving, an electric razor is preferable when using warfarin.

Side effects

Bleeding is the most important complication of warfarin. Other possible side effects include nausea, vomiting, diarrhoea, rash and skin necrosis (usually occurs on days 3 to 8 of therapy). Skin necrosis is an extremely rare side effect of warfarin however if it occurs treatment must be obtained immediately. Skin necrosis is basically death of skin tissue and usually starts with red skin. Other possible side effects include alopecia (hair loss) and purple toe syndrome. Purple toe syndrome is a rare condition caused by warfarin that can occur in the first few weeks of warfarin treatment and is caused by deposits of cholesterol collecting in the toes. Usually the big toe only is affected and it is characterised by a blueish or purple colour and sometimes pain. Warfarin may need to be stopped if it occurs. Jaundice (yellowing of skin and whites of eyes) is a sign of liver problems so must be investigated immediately if taking warfarin.

Interactions

Warfarin interacts with more medication and foods than most drugs. Many drugs **increase** the effect of warfarin thus increasing the risk of bleeds. These include antifungal medication such as fluconazole (Diflucan[®]) and itraconazole (Sporanox[®]) and antibiotics such as clarithromycin (Klacid[®]), erythromycin, metronidazole (Flagyl[®]), ciprofloxacin (Ciproxin[®]) and tetracycline. Other drugs which increase the effect of warfarin include NSAIDs (anti-inflammatory pain killers like ibuprofen), amiodarone (Cordorone X[®]) which is used for irregular heart beat, cimetidine and omeprazole (Losec[®]) which are used for stomach ulcers, phenytoin (Epanutin[®]) which is used for epilepsy, simvastatin (Zocor[®]) which is used for cholesterol, tamoxifen which is used for breast cancer and thyroxine which is used for underactive thyroid. Some herbs increase the effect of warfarin including ginkgo biloba and devil's claw. Some drugs **reduce** the effect of warfarin including some sedatives, carbamazepine (Tegretol[®]) which is used for epilepsy and trazodone (Molipaxin[®]) which is used for depression. Herbs that reduce the effect of warfarin include ginseng and green tea.

How long does warfarin need to be taken for?

The length of warfarin depends on many factors. It can vary from a few days to prevent a clot after a hip replacement to lifetime treatment for somebody treated with a mechanical heart valve. Every case is different, so how long warfarin needs to be taken is determined on a case by case basis. For example, someone who has a long term risk of clots such as atrial fibrillation will need to take it for at least six months.

Surgery

To reduce the risk of bleeding during surgery, warfarin is sometimes discontinued for a few days before surgery. The European Society of Cardiology recommends that for major surgical procedures an INR of 2.0 or below is required.

This may require discontinuation of warfarin for several days with the patient changed to heparin instead before and after elective surgery as heparin does not have a risk of bleeds. Generally, for patients with a low risk of clot, warfarin will be stopped 5 days prior to surgery. For patients with a high risk of clot, warfarin will be stopped 4 days before surgery and substituted with heparin. In both cases, warfarin is usually restarted as soon as oral fluids are tolerated by the patient after surgery.

Disclaimer: Please ensure you consult with your healthcare professional before making any changes recommended

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