WARFARIN (COUMADIN)

WHAT IS WARFARIN?

Warfarin (Coumadin) is a prescription medication that inhibits normal blood clotting (coagulation). Because it interferes with the formation of blood clots, it is also called an anticoagulant. Many people refer to these kinds of medicines as blood thinners, although they do not actually cause the blood to become less thick, only less likely to clot.

The normal clotting mechanism is a complex process that involves multiple substances (clotting factors). These factors are produced by the liver and act in sequence to form a blood clot. In order for the liver to produce a number of the clotting factors, adequate amounts of vitamin K must be available. Warfarin blocks the availability of vitamin K, and limits the production of these clotting factors. As a result, the clotting mechanism is disrupted and it takes longer for the blood to clot.

USES

Normally when body tissues are cut or traumatized, the blood clots in order to prevent excessive blood loss. In some patients, however, the clotting mechanism may be triggered by other factors, leading to the formation of small clots (thrombi) in the bloodstream. These clots may travel through the bloodstream and become lodged in smaller blood vessels, reducing blood flow to the organs supplied by those vessels. Blockage of blood flow can cause serious problems including stroke (when a blood vessel leading to a portion of the brain is blocked) and heart attack (when a blood vessel leading to the heart is blocked).

Warfarin is prescribed for patients who are at increased risk for developing harmful blood clots. Patients at risk for developing such clots include those with a mechanical heart valve, an irregular heart rhythm called atrial fibrillation and patients with certain clotting disorders.

Warfarin is also used in patients who have previously developed harmful clots, including patients who have had a stroke, heart attack, a clot which has traveled to the lung (pulmonary embolism), or a blood clot in the leg (deep venous thrombosis or DVT). In addition, warfarin may be used to prevent an existing clot from growing larger.

MONITORING

The goal of warfarin therapy is to decrease the clotting tendency of blood, but not to prevent clotting completely. Therefore, the effect of warfarin on the blood's ability to clot must be carefully monitored with periodic blood testing. Based on the results of these tests, the dose of warfarin is adjusted to maintain the clotting time within a target range.

Prothrombin time (PT)

The test most commonly used to measure the effects of warfarin is the prothrombin time (called pro time, or PT). The PT is a laboratory test that measures the time it takes for the clotting mechanism to progress. It is particularly sensitive to the clotting factors affected by warfarin. The PT is also used to compute a value known as the INR (or International Normalized Ratio).

International Normalized Ratio (INR)

The INR is a way of expressing the PT in a standardized way; this ensures that results obtained by different laboratories can be reliably compared.

The longer it takes the blood to clot, the higher the PT and INR. The target INR range depends upon the clinical situation. In most cases the target range will be 2 to 3, although other ranges may be chosen if there are special circumstances. If, at any particular time, the INR is below the target range (i.e., under-anticoagulated), there is a risk of clotting. If, on the other hand, the INR is above the target range (i.e., over-anticoagulated), there is an increased risk of bleeding.

Dosing

When warfarin is first prescribed, a higher loading dose may be given so that an effective blood level of the drug is achieved quickly. The loading dose is then adjusted downward until a maintenance dose is found that maintains the INR within the desired range. The PT and INR are monitored frequently until the maintenance dose has been determined. Once the patient is on a stable maintenance dose, the PT and INR are monitored less frequently, generally once every two to four weeks.

The warfarin dose may be adjusted periodically in response to a changing INR or to clinical circumstances that call for an increase or decrease in warfarin therapy. For example, having surgery may require a change in a patient's warfarin regimen. The dose of warfarin may also be modified if other medicines are taken.

SIDE EFFECTS

The major complication associated with warfarin is bleeding due to excessive anticoagulation. Excessive bleeding, or hemorrhage, can occur from any area of the body, and patients on warfarin should report any falls or accidents, as well as signs or symptoms of bleeding or unusual bruising. Signs of unusual bleeding include bleeding from the gums, blood in the urine, bloody or dark stool, a nosebleed, or vomiting blood. Because the risk of bleeding increases as the INR rises, the INR is closely monitored and adjustments are made as needed to maintain the INR within the target range.

When to seek help

If there are obvious or subtle signs of bleeding, including the following, patients should call their healthcare provider immediately.

- Persistent nausea, gastrointestinal upset, or vomiting blood or other material that looks like coffee grounds
- Headaches, dizziness, or weakness
- Nosebleeds
- Dark red or brown urine
- Blood in the bowel movement or dark-colored stool
- Pain, discomfort, or swelling, especially after an injury
- After a serious fall or head injury, even if there are no other symptoms

The patient should also call if any of the following occurs:

- Bleeding from the gums after brushing the teeth
- Swelling or pain at an injection site
- Excessive menstrual bleeding or bleeding between menstrual periods
- Diarrhea, vomiting, or inability to eat for more than 24 hours
- Fever (temperature greater than 100.4° F or 38° C)

It is important to remember that warfarin is taken to reduce of one of a number of clotting conditions. The features of a blood clot are discussed within the appropriate topic review. If one or more of these symptoms develops, the patient should seek immediate medical attention.

PREGNANCY AND WARFARIN

Warfarin is not recommended during pregnancy, especially during the first trimester, due to an increased risk of miscarriage and birth defects. A patient who becomes pregnant or plans to become pregnant while on warfarin therapy should notify their healthcare provider immediately.

OTHER RECOMMENDATIONS

Take warfarin on a schedule — Warfarin should be taken exactly as directed. Do not increase, decrease, or change the dosing schedule unless told to do so by a healthcare provider. If a dose is missed or forgotten, call the prescribing clinician for advice.

Warfarin tablets come in different strengths; each is usually a different color, with the amount of warfarin (in milligrams) clearly printed on the tablet. If the color or dose of the tablet appears different than those taken previously, the patient should immediately notify their pharmacist or healthcare provider.

Reduce the risk of bleeding

There is a tendency to bleed more easily than usual while taking warfarin. Some simple changes can decrease this risk:

- Use a soft bristle toothbrush
- Floss with waxed floss rather than unwaxed floss
- Shave with an electric razor rather than a blade
- Take care when using sharp objects, such as knives and scissors
- Avoid activities that have a risk of falling or injury (e.g. contact sports)

Prevent falls

Falling may significantly increase the risk of bleeding. Taking measures to prevent falls is recommended, and could include the following:

- Remove loose rugs and electrical cords or any other loose items in the home that could lead to tripping, slipping, and falling.

- Ensure that there is adequate lighting in all areas inside and around the home, including stairwells and entrance ways.

- Avoid walking on ice, wet or polished floors, or other potentially slippery surfaces.

- Avoid walking on unfamiliar areas outside.

Warfarin and food

Some foods and supplements can interfere with warfarin's effectiveness. After being stabilized on a particular warfarin dose, consult a healthcare provider before making major dietary changes (e.g., starting a diet to lose weight, starting a nutritional supplement or vitamin).

- Vitamin K— Eating an increased amount of foods rich in vitamin K can lower the prothrombin time and INR, making warfarin less effective, and potentially increasing the risk of blood clots. Patients who take warfarin should aim to eat a relatively similar amount of vitamin K each week. Some foods have a high level of vitamin K, including: kale, broccoli, spinach, collard or turnip greens, lettuce, Brussels sprouts, and cabbage (See Table 1). It is not necessary to avoid these foods. However, the patient should eat a relatively similar amount on a regular basis rather than eating a large serving occasionally.

- Cranberry juice — There have been mixed reports on the effect of cranberry juice in people who use warfarin to prevent blood clots. Some experts have reported that drinking cranberry juice while on warfarin can cause significant over anticoagulation and bleeding. However, a small study found that drinking one eight ounce serving of cranberry juice per day for seven days had no effect on the

INR of seven men taking warfarin for atrial fibrillation. It is plausible that larger amounts could have a more significant effect. The best advice is probably to avoid consuming large amounts of cranberry juice, and to speak with a healthcare provider regarding any concerns about a possible interaction.

- Alcohol — Chronic abuse of alcohol affects the body's ability to handle warfarin. Patients on warfarin therapy should avoid drinking alcohol on a daily basis. Alcohol should be limited to no more than one to two servings of alcohol occasionally. In addition, drinking excessive amounts of alcohol can increase the risk of injury, and therefore bleeding.

Table 1: Foods with moderate to high levels of vitamin K

Food name	Serving size	Vitamin K (micrograms)
High level vitamin K foods		
Kale, frozen (cooked or boiled, drained)	1/2 cup	570
Kale, fresh, (cooked or boiled, drained)	1/2 cup	530
Spinach, frozen (cooked or boiled, drained)	1/2 cup	514
Spinach, raw	1 cup	150
Collard greens, frozen (cooked, drained)	1/2 cup	530
Turnip greens, frozen (cooked, drained)	1/2 cup	425
Brussels sprouts, frozen (cooked, drained)	1/2 cup	110
Moderate level vitamin K foods		
Asparagus, frozen (cooked, drained)	1/2 cup 4 spears	72 48
Asparagus, fresh (cooked, drained)	4 spears	30
Broccoli, frozen (cooked, drained)	1/2 cup	60
Broccoli, fresh (cooked, drained)	1 spear	52
Broccoli, raw	1/2 cup	40
Lettuce (butterhead, Boston, bibb)	1/2 head	80
Lettuce (iceberg, crisphead)	1/2 head	65
Lettuce (romaine, cos)	1 cup	57

Lettuce (green leaf)	1 cup	97
Okra, fresh (cooked, drained)	1/2 cup	32
Okra, frozen (cooked, drained)	1/2 cup	44
Cabbage (cooked, drained)	1/2 cup	73
Cabbage, raw	1/2 cup	21
Cabbage, savoy (raw)	1/2 cup	24
Cabbage, Chinese (cooked, drained)	1/2 cup	28
Coleslaw (fast food-type)	3/4 cup	56
Sauerkraut, canned	1/2 cup	41
Peas, frozen, with pod (cooked, drained)	1/2 cup	24
Peas, fresh, with pod (cooked, drained)	1/2 cup	20
Peas, green, frozen (cooked, drained)	1/2 cup	18
Celery, raw	1/2 cup	17
Beans, green or yellow, fresh (cooked, drained)	1/2 cup	10
Oil, canola	1 tablespoon	17
Oil, olive	1 tablespoon	8
Oil, other (including peanut, sesame, safflower, corn, sunflower, soybean)	1 tablespoon	3 or less
Green tea, brewed in hot water	3.5 ounces	0.3

Warfarin and medications

A number of medications, herbs, and vitamins can interact with warfarin (see Table 2). This interaction may affect the action of warfarin or the other medication. If warfarin is affected, the dose may need to be adjusted (up or down) to maintain an optimal coagulation effect.

Patients who take warfarin should consult with their clinician before taking any new medication, including over-the-counter (non-prescription) drugs, herbal medicines, vitamins, or any other products. Some of the most common over-the-counter pain relievers, including acetaminophen (Tylenol), aspirin, and nonsteroidal anti-inflammatory

drugs (such as ibuprofen [Advil] and naproxen [Aleve]) enhance the anticoagulant effects of warfarin. Vitamin E may increase the anticoagulant effects of warfarin. Consult a healthcare provider before adding or changing a dose of vitamin E or any other vitamin.

Table 2: Medications that interfere with warfarin

Increased warfarin effect	Decreased warfarin effect
Acetaminophen	Azathioprine
Allopurinol	Antithyroid drugs
Aspirin	Carbamazepine
Amiodarone	Dicloxacillin
Capecitabine	Glutethimide
Cephalosporins	Griseofulvin
Cimetidine	Haloperidol
Ciprofloxacin	Nafcillin
Clofibrate	Oral contraceptives
Clopidogrel	Phenobarbital
Diclofenac	Rifampin
Disulfiram	Vitamin K
Erythromycin	
Fluconazole	
Fluorouracil (5-FU)	
Fluoxetine	
Glucagon	
Influenza virus vaccine	
Metronidazole	
Macrolide antibiotics	
Omeprazole	

Sulfamethoxazole/trimethoprim
Tamoxifen
Thyroid hormone
Tolbutamide