



ORAL ANTICOAGULANT THERAPY: PRACTICAL GUIDE FOR PATIENTS AND THEIR FAMILIES

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INTRODUCTION

This guide is aimed at all patients who follow therapy with oral anticoagulant medicines (OAT).

WHAT ARE ORAL ANTICOAGULANTS?

Coagulation is a protective mechanism: when we accidentally injure ourselves, the blood stops flowing thanks to the interaction of the coagulation factors and platelets which form a "plug", the so-called thrombus.

Oral or dicoumarol anticoagulants (Warfarin- Coumadin and Acenocoumarol- Sintrom) are medicines capable of modifying the ability to clot blood and reduce the risk of thrombus formation in patients who run this risk due to their disease.



SINTROM tablets
1 mg or 4 mg



COUMADIN tablets
5 mg

WHAT ARE ORAL ANTICOAGULANTS USED FOR?

OAT is used to keep the blood more fluid so as to reduce the risk of formation of thrombi and clots inside the blood vessels (veins and arteries).

HOW DO ORAL ANTICOAGULANTS WORK?

Their action is based on the interference with the activation of some substances (coagulation factors) which are used for the formation of a clot; as in fact they need vitamin K to be active. Oral anticoagulants inhibit the action of this vitamin

and therefore, indirectly, make the blood less coagulable. There is therefore antagonism between dicumarols (Coumadin and Sintrom) and vitamin K, which can therefore be used as an antidote in case of excessive dosage of anticoagulant medicines. The vitamin K in our body is partly introduced with food and partly directly produced in our intestines by the germs that normally live there; this allows us to always have the necessary quantity.

HOW MUCH MEDICINE IS NEEDED?

Anticoagulant medicines cannot be administered in fixed doses as is the case with other medicines. Each patient requires an individualized dose of medication to achieve the appropriate level of anticoagulation. In fact, if on the one hand these medicines prevent the formation of thrombi, on the other, they expose the patient to an increased risk of haemorrhage.



**Insufficient dose of medicine =
too thick blood = risk of
thrombosis**

**Excessive dose of medicine =
too fluid blood = risk of bleeding**

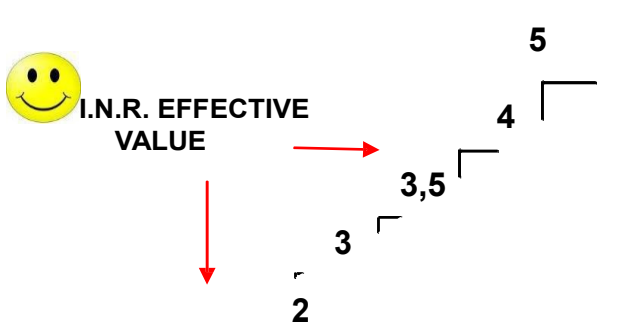


Effective dose of medicine = fluid blood = thrombosis prevention without risk of haemorrhage

HOW IS THE EFFECTIVENESS OF ORAL ANTICOAGULANTS MEASURED?

The action of these medicines causes a slowdown in the clot-forming ability. Their effect is highly variable between different individuals and can vary over time even for the same individual. In other words, the amount of the medicine needed per person can be very different, with doses even ten times greater from one individual to another. Therefore, to evaluate the effectiveness of the medicine, it is necessary to refer not to the amount taken but to a laboratory test that measures the time that the blood takes to clot. This time is measured in the blood through a test called Prothrombin Time (PT), which we usually find expressed as a percentage (prothrombin activity) or as **INR**. The INR represents the safest and most correct index we have.

This is a ratio between the patient's prothrombin time and the prothrombin time of a mixture of normal plasma raised to the power of the ISI (International Sensitivity Index): the result is a number that identifies the sensitivity of the single kit used in the laboratory. All of this is expressed by the formula: $INR = \text{patient PT} / \text{normal subject PT}$.



WHY SHOULD YOU TAKE ORAL ANTICOAGULANTS?

There are some clinical conditions that have an indication for treatment with oral anticoagulants. TAO is useful in diseases that can be complicated by the formation of "thrombi"/"blood clots" which detach from their site and cause embolisms in the arteries, hindering blood circulation with very serious consequences.

Table 1 shows a list of these conditions with the therapeutic range of INR values (range) and the optimal value (Target) next to them.

Table 1: indications for anticoagulant therapy and range of INR and coagulation target.

PATHOLOGY	THERAPEUTIC RANGE	TARGET
Prophylaxis of venous thromboembolism	1.5-2,5	2
Treatment of DVT/PE, atrial fibrillation	2-3	2,5
Valvulopathies, dilated cardiomyopathy	2-3	2,5
Biological valve prostheses	2-3	2,5
Heart attack	2-3	2,5
RS aortic double hemidisk valve prostheses	2-3	2,5
Mechanical valve prostheses	2,5-3,5	3
Antiphospholipid antibody syndrome	3-4	3,5

INTERACTIONS WITH OTHER MEDICINES

It may happen that you need to take other medicines in addition to oral anticoagulants. It must be borne in mind that other medicines can modify the response to anticoagulant medicines, sometimes with an increase, sometimes with a decrease in the INR. Therefore it is necessary to reduce the use of other medicines to the bare essentials, trying to use those known to be safe. However, it is important to know that in case of need any medicine can be used, with attention to carrying out more frequent checks of the INR if it is known that this medicine can

interfere with oral anticoagulants or, as very often happens, when one is not sure of the effects it can cause. We recommend following the advice given in the therapy booklet which include:

As an antipyretic: PARACETAMOL

As a pain reliever: IBUPROFEN

As an antibiotic: AMOXICILLIN

The injection of medicines intramuscularly should be avoided, because deep hematomas can be created in the muscle, which can be very annoying. Concerning vaccinations, they can be performed regularly, taking care to give the injection under the skin. In particular, there are no risks in carrying out the flu vaccination.

Below you will find in **table 2** the major pharmacological interactions between anticoagulants and commonly used medicines.

Table 3 shows medicines that can be safely taken by patients under oral anticoagulant therapy.

Table 2: Clinically relevant drug interactions

Antibiotics	Cardiovascular	Antiphlogistics-analgesics	CNS	GI	Miscellaneous
Potentialiation of oral anticoagulant therapy: Co-trimoxazole Ciprofloxacin Erythromycin Fluconazole Isoniazid Metronidazole Miconazole Tetracyclines	ASA extension Amiodarone quinidine Fibrati Propafenone Propranolol Simvastatin Sulfinipyrazone Ticlopidine	Piroxicam Phenylbutazone		Cimetidine Omeprazole	Tamoxiphene Danazol
Inhibition of oral anticoagulant therapy: Rifampicin Nafcillin	Cholestyramine		carbamazepine Phenobarbital Phenyntine	sucralfate	Vitamin K

ASA=acetylsalicylic acid

GI=gastrointestinal

CNS = central nervous system

Table 3: Relatively safe drugs

Antibiotics	Cardiovascular	Antiphlogistics-analgesics	CNS	GI	Miscellaneous
Penicillins	Atenolol Disopyramide Flecainides Lidocaine Calcium channel blockers Furosemide ACE inhibitors Pravastatin Digoxin	Paracetamol	Benzodiazepines Tricyclics SSRIs Sodium valproate Ethosuccinamide	Ranitidine Pantprazole	Metformin Flu vaccination

SSRIs = selective serotonin release inhibitors



THE DIET

If you maintain a regular diet, there will be very rarely alterations in the response to anticoagulants that depend on the diet.

Avoid taking incongruous quantities of alcohol in any form (wine, beer, spirits).

Consult your doctor in case of slimming diets.

In general, avoid broad leafy vegetables rich in vitamin K (see table). Pay attention to herbal products.

In this case it will be necessary to shorten the interval between INR checks for a few weeks. Therefore, no food should be considered "forbidden" in absolute terms.

AVOID: parsley (allowed only as an "ornament"), savoy cabbage;

ATTENTION: broccoli, sprouts, cabbage, spinach, turnip greens, sprouts, lettuce, other green salad, liver (try to take the same amount avoiding variations in the dose greater than 100 g compared to the usual consumption of these foods).

Below the table shows some of the foods richest in vitamin K which have to be avoided in large quantities by patients taking dicoumarols.

Table 4: Foods rich in vitamin K

Dried basil	Fresh basil
Dried thyme	Chicory
Dried sage	Broccoli
Raw parsley	Radish
Cabbage	Endive
Dried oregano	Brussels sprouts
Dried marjoram	Soybean oil
Spinach	Lettuce
Turnip	Cabbage
Beets	

Table 5: Interactions between herbs and oral anticoagulants

<p>ENHANCE THE ANTICOAGULANT EFFECT: Ganoderma japonicum, Salvia miltiorrhiza, Ginko, China, Garlic, St. John's wort, White willow, Spirea, Tamarind</p>
<p>DECREASE THE ANTICOAGULANT EFFECT: passion flower, juniper, Medicinal verbena, Ginseng</p>



ONSET OF OTHER DISEASES

In case of other diseases, it will be necessary to intensify the number of INR checks, in the case of important and/or prolonged episodes, or in the case of diarrhea and vomiting or thyroid disease. If these conditions determine the need to use other medicines, please refer to what has been said in the paragraph [interactions with other medicines](#).

HOW AND WHEN TO TAKE ANTICOAGULANTS?

Coumadin or Sintrom are taken once a day, preferably between meals, in the central hours of the afternoon or in the evening before going to bed. However, it is advisable to always take the medicine at the same time. It is advisable to carefully record the doses taken in a booklet (the day and the amount of medicine) in order to reduce the possibility of error, which is greater as the dose is often modified for the adjustment necessary to maintain the correct INR.

The INR check must be performed regularly, according to the indications of your doctor; you may be asked at the start of therapy to closely monitor your INR (2-3 times a week) in order to identify the dose of medicine needed to bring your blood into the right coagulation interval (range). After 2-3 months the controls can be reduced and can be performed once a month.

HOW CAN I CHECK THE INR VALUE?

In order to calculate the INR value, a blood sample is required.

IT IS NOT NECESSARY TO FAST BEFORE INR BLOOD TEST.

FACILITATION for INR blood test:

You can acquire the exemption from payment for related pathologies;

Cumulative prescription for 8 samples so as to avoid repeated visits to the family doctor;

INR result after a few hours

Immediate warning by the laboratory if INR exceeds the alarm values



RISKS OF ORAL ANTICOAGULANT THERAPY

Hemorrhages

Since anticoagulant medicines delay the normal blood clotting process, it is possible that bleeding from the gums, nose or hemorrhoids may appear during treatment; moreover, bruises can easily form on the skin even for small traumas. On the other hand, the times for repairing small wounds or grazes are usually normal and it is not necessary to take particular precautions in carrying out daily activities. Major vaginal bleeding usually only appears if there are pathologies of the uterus such as fibroids. An accurate gynecological evaluation is therefore necessary in this eventuality. In the event of major trauma, it is necessary to check the INR even if there is no obvious bleeding: a deep injury can cause hidden bleeding, therefore an INR value that is too high at that moment can be more dangerous than it is in usual conditions. Every time you go to a doctor for any problem, you must point out that you are taking an

anticoagulant medicine; this will be of greater importance precisely in the Emergency Room.

Table 4: Management of overdose situations:

1) INR greater than 5 without bleeding	→ reduce or suspend the therapy for 1-3 days
2) INR greater than 5 with minor bleeding	→ suspend for 1-3 days then check INR → vitamin K 0.5-2 mg orally then urgent blood count check
3) Non-serious bleeding with INR in range	→ check local causes before suspending
4) Major bleeding (CNS, gastrointestinal, retroperitoneal) with any INR	→ suspend + vitamin K 5-10 mg by slow intravenous route (anaphylactic shock risk)

Thrombosis

If the anticoagulant therapy is well conducted and the INR is kept within the desired range, the anticoagulant medicines protect against the formation of thrombi. However, exceptionally, in periods of poor control of the therapy or due to the appearance of other disease conditions not present up to then, symptoms referable to the formation of thrombi may appear. It is therefore necessary to immediately determine the INR and promptly seek medical attention.

Table 7: Absolute contraindications to oral anticoagulant therapy

PREGNANCY	Risk of malformations in the first trimester, bleeding risk for the newborn in the first 4-6 weeks
RECENT MAJOR BLEEDING	<p>All bleeding events occurring intracranially, intraocular with visual impairment, retroperitoneal, intraarticular</p> <p>All events that require surgical treatment</p> <p>All events that lead to a reduction in HB of 2 g/dl or that make blood transfusions necessary</p>

Table VIII: Conditions at high risk of complications

POOR COOPERATION	Psychiatric diseases, involutionary states of the brain, degenerative brain diseases
CARDIOVASCULAR DISEASES	Severe arterial hypertension, bacterial endocarditis, pericarditis, heart failure
KIDNEY DISEASES	Severe renal insufficiency
NEUROLOGICAL DISEASES	Recent non-embolic vascular accident, aneurysms, AVMs, CNS trauma

GASTROINTESTINAL DISEASES	Haemorrhagic colitis, active gastric ulcers, oesophageal varices
LIVER DISEASES	Severe hepatic insufficiency, cholestatic jaundice
HEMATOLOGICAL DISEASES	Qualitative or quantitative alterations of platelets

Table 9

FACTORS CONDITIONING A PARTICULARLY HIGH BLEEDING RISK DURING ORAL ANTICOAGULANT THERAPY:

- Age greater than 85 years
- History of major bleeding
- Tendency to fall
- Difficulty maintaining INR in therapeutic range (INR>4.5)
- Poor cooperation with therapy
- Difficulty following the patient



OTHER SPECIAL CONDITIONS

Pregnancy, breastfeeding

All oral anticoagulant medicines cannot be used during pregnancy, as they are dangerous for the baby because they pass the placental barrier. It is therefore necessary that women of childbearing age avoid becoming pregnant while taking this therapy; if they have doubts about a possible pregnancy, they should immediately take a test to ascertain it and contact the doctor, so that oral anticoagulants can be discontinued within the 6th week of pregnancy. If a pregnancy is desired, the anticoagulant medicines must be replaced with heparin with subcutaneous injections 2-3 times a day. This treatment is not dangerous and should be continued until delivery. Women being treated with oral anticoagulants can instead breastfeed, without this causing any risk to the baby.

Travelling, sports

There is no limitation regarding the possibility of traveling. It should only be kept in mind that this usually accompanies changes in eating habits, so it is advisable, if possible, to vary the way the patient eats slightly, or alternatively to carry out more frequent INR checks. It is advisable to avoid sports that may expose you to the risk of serious trauma, such as downhill skiing or acrobatic gymnastics. No special precautions are required for all other activities.

Since discharge from hospital...

If you have just been discharged from hospital and have been prescribed an anticoagulant medicine, [trust your family doctor and contact him/her](#), s/he will explain the closest place to take the blood sample and will help you manage the dosage of the therapy in order to reach your target as quickly as possible.

Requests for a cycle of INR blood tests are made by the family doctor.

Blood samples for INR are taken at:

- Health Districts
- Cattinara hospital sampling center
- Collection center at the Maggiore Hospital
- Cardiovascular Center
- Private laboratories, as long as the result is expressed in INR

At home – always through your Health District and with the request of the family doctor.

Autonomous management of anticoagulation (home self-monitoring)

There is a coagulometer (Coagucheck) for sale, i.e. a device with which the patient manages the therapy independently. This device avoids traumatism of the veins and allows greater autonomy for patients (travel, weekends).

The start of oral anticoagulant therapy is the most delicate moment of the whole treatment as it is often not easy to reach the maintenance dose. The attack (start) dose should be close to the maintenance dose. Only in young patients it is started with high doses of warfarin (10mg), more often it is started with 5mg and in elderly patients with a lower dose (2.5mg).

SPECIAL SITUATIONS WHEN IT IS NECESSARY TO CONTACT YOUR DOCTOR

- Before tooth extractions or other dental procedures;
- Before endoscopic investigations of the gastrointestinal or urinary tract (gastroscopies, colonoscopies, cystoscopies, etc.);
- Significant change of the usual state of health (in particular diarrhea, vomiting, pain and fever);
- When you have to take medicines other than the usual ones not included in the list of "safe" medicines or if you stop or change the dosage of a medicine you have been taking for a long time;
- When mistakes have been made in taking anticoagulant

medication

- If you have blood in the urine, nosebleeds with difficulty stopping the bleeding, gross bruising due to small or spontaneous traumas, very abundant blood in the stools or black stools, very abundant menstruation compared to the usual flow.
- In case of major traumas even without apparent damage, especially to the head and/or back.

NB: All patients with heart valve prostheses or heart valve disease must ask their doctor for precise instructions on the prevention of endocarditis by taking antibiotics; this prevention is always necessary to carry out the procedures listed above.

Have blood samples taken regularly to check blood coagulation according to your doctor's instructions

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