

INR (International Normalised Ratio)

INR is a standard test that measures how long blood takes to clot. Normally, blood that is not anticoagulated, has an INR of approximately 1.0. The dose of anticoagulant that a patient needs to take will depend on the INR test result. If the result is out of the range appropriate for the condition, the dose of anticoagulant needs to be increased or decreased accordingly. The anticoagulant dose required to achieve the target INR varies for each person.

Clinical indications

The most common clinical indications for oral anticoagulation are atrial fibrillation, treatment and prevention of deep vein thrombosis/venous thromboembolism, and heart valve prostheses. A comprehensive review of clinical indications for oral anticoagulants is included in the British Society for Haematology Guidelines (www.bcshguidelines.com).

Anticoagulation is not indicated for the following conditions: ischaemic stroke without atrial fibrillation, retinal vessel occlusion, peripheral arterial thrombosis, coronary artery graft or coronary angioplasty and stents.

The maintenance period and the target INR can vary. The most common indications are shown in table 1 below:

Table 1: Indications, target INR and duration of anticoagulation

INDICATION	TARGET INR	DURATION OF ANTICOAGULATION
Pulmonary embolus	2.5	6 months
Proximal deep vein thrombosis	2.5	6 months*
Calf vein thrombus	2.5	3 months
Recurrence of venous thromboembolism when no longer on warfarin therapy	2.5	Consider long-term
Recurrence of venous thromboembolism whilst on warfarin therapy	3.5	Consider long-term
Antiphospholipid syndrome	2.5	Consider long-term
Atrial fibrillation	2.5	Long-term
Cardioversion	2.5	3 weeks before and 4 weeks after procedure
Mural thrombus	2.5	3 months
Cardiomyopathy	2.5	Long-term
Mechanical prosthetic heart valve	2.5 – 3.5**	Long-term

*Shortening treatment to 3 months will be recommended if circumstances indicate that the risk benefit ratio favours this, for example if a reversible precipitating factor was present and there are risk factors for bleeding (age > 65 years).

**Depending on valve type and/or location. See www.bcshguidelines.com/pdf/oralanticoagulation.pdf section 3.8 for further details.

Ongoing monitoring

Once a patient has a stable INR, the recall interval can be progressively lengthened and this is built into many computerised dosing support systems. Table 2 shows a suggested schedule for recall frequency for manual recall.

Table 2: Warfarin therapy – maximum recall periods during maintenance therapy*

One INR high:	Recall in 7–14 days (stop treatment for 1-3 days; maximum 1 week in prosthetic valve patients)
One INR low:	Recall in 7–14 days
One INR therapeutic:	Recall in 4 weeks
Two INRs therapeutic:	Recall in 6 weeks (maximum for prosthetic valve patients)
Three INRs therapeutic:	Recall in 8 weeks, apart from prosthetic valve patients
Four INRs therapeutic:	Recall in 10 weeks, apart from prosthetic valve patients
Five INRs therapeutic:	Recall in 12 weeks, apart from prosthetic valve patients

Note: Patients seen after discharge from hospital with prosthetic valves may need more frequent INR monitoring in the first few weeks (based on data from Ryan et al. *British Medical Journal*. 1989; 299: 1207-1209).

*Taken from the BMA outline for the National Enhanced Service – anticoagulation monitoring.

SAFER PRACTICE TIP

Changes in drug treatment, clinical status, diet, alcohol intake or non-adherence to the prescribed/agreed regimen can all alter INR. Patients and carers should be encouraged to tell the clinic or person who is responsible for warfarin prescribing about any changes that could potentially affect the INR and warfarin dose requirements so that extra INR monitoring can be undertaken.

Drug interactions

Numerous drugs interact with warfarin and the British National Formulary contains a useful list.

Warfarin is metabolised by cytochrome p450 2C9 (CYP2C9). Patients with liver disease or those taking drugs that inhibit the activity of CYP2C9 (for example macrolide antibiotics and quinolones) will require less warfarin. Patients taking drugs that accelerate the metabolism of warfarin (for example, rifampicin, barbiturates and carbamazepine) will require more warfarin.

Table 3: Drug interactions*

AVOID	
Aspirin	Except where combination specifically indicated for example mechanical valve prosthesis, recurrent thrombosis
Analgesics	Co-proxamol, ketorolac (post-operative)
Antifungals	Miconazole
Diabetes	Glucagon
Non steroidal anti-inflammatory drugs	Azapropazone, phenylbutazone
Others	Enteral feeds containing vitamin K
ADJUST DOSE	
Ulcer healing	Cimetidine, omeprazole
Antiarrhythmics	Amiodarone, propafenone
Lipid lowering	Fibrates
Antiepileptics	Carbamazepine, phenobarbitone, phenytoin, primidone
Dependency	Disulfiram
Antibiotics/antifungals	Aztreonam, cefamandol, chloramphenicol, ciprofloxacin, co-trimoxazole, erythromycin, griseofulvin, metronidazole, ofloxacin, rifampicin, sulphonamides
Thyroid	Carbimazole, thiouracils, thyroxine
Non steroidal anti-inflammatory drugs	Diflunisal
Gout	Allopurinol, sulphinyprazole
Others	Aminoglutethimide, barbiturates, ciclosporin, mercaptopurine, oral contraceptive steroids
MONITOR INR	
G.I. motility	Cisapride
Antiarrhythmics	Quinidine, amiodarone
Lipid lowering	Colestyramine, statins
Antidepressants	Serotonin uptake antagonists
Antibiotics/antifungals	Consult BNF if not listed under 'adjust dose'
Diabetes	Tolbutamide
Non steroidal anti-inflammatory drugs	If not listed under 'avoid' or 'adjust dose'
Others	Anabolic steroids, corticosteroids, hormone antagonists, ifosfamide, influenza vaccine, Rowachol, sucralfate

*This list is not exhaustive: if in doubt consult the British National Formulary.