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All information is intended for use by competent health care professionals and should be utilised in conjunction with pertinent clinical data.

Contents

Key Messages

- To ensure safe and effective anticoagulation, a systematic and practice-wide approach is needed for warfarin therapy and for the maintenance of INR levels within appropriate target ranges. You can test your practice systems with the bpac^{nz} practice audit for INR monitoring

- Patients who are well informed and understand what they are doing are more likely to benefit from treatment; therefore effective patient education is an important component of achieving good INR levels.

- Regular testing of INR levels is essential for all people taking warfarin. For most people once the INR is stable the rate of INR testing can be extended to two weekly and then 4 to 6 weekly. However people with higher levels of risk, may need more frequent testing.

1. Introduction

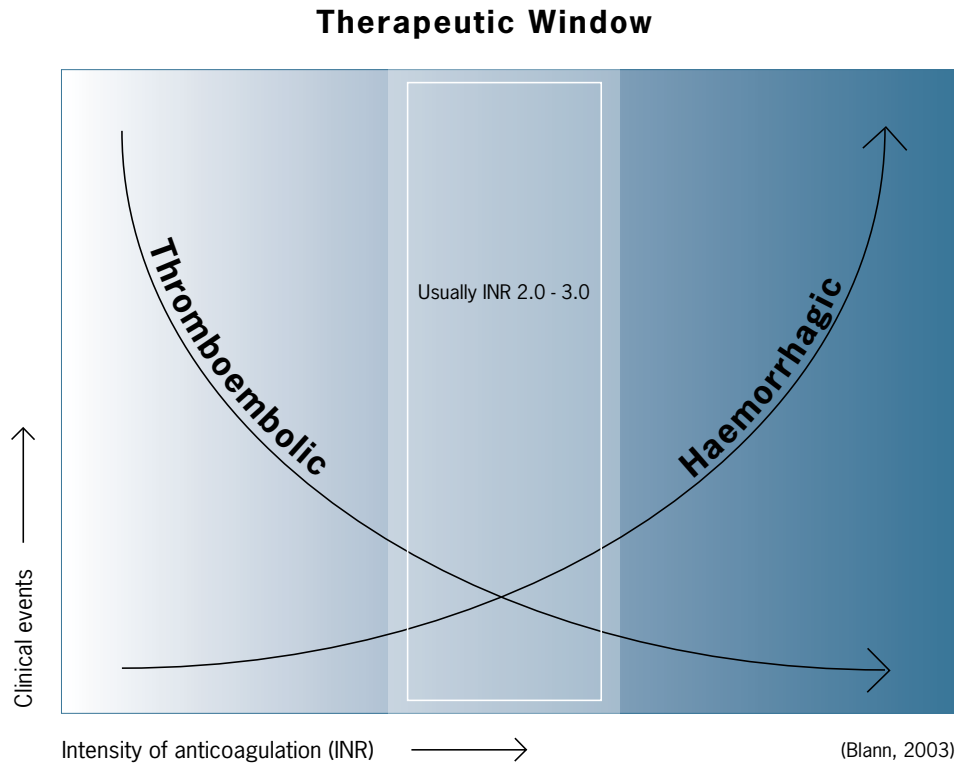
Warfarin is the most widely used anticoagulant in New Zealand. It has a valuable role in the prevention of thrombosis but the use of warfarin is associated with serious risks. Warfarin is the most frequent cause of adverse drug reactions in New Zealand (Didham, 2006).

To ensure safe and effective anticoagulation, a systematic and practice-wide approach is needed for warfarin therapy and the maintenance of INR levels within appropriate target ranges.

Good management of INR levels requires a systematic approach involving the whole practice team.

1a. The role of INR

INR testing is used to maintain warfarin response within the therapeutic window. Maintaining the INR within a target range is the key to minimising the risks of bleeding while providing the benefits of anticoagulation (Blann, 2003).



1b. What is INR?

The basis of the INR is the one-stage prothrombin time (PT) using the reagent thromboplastin. In the past, PT values varied dependent on the particular thromboplastin used. To avoid this, all thromboplastins are now standardised against a WHO standard, and are assigned an International Sensitivity Index (ISI). This enables the International Standardised Ratio (INR) to be calculated. The development of INR has enabled patients on warfarin therapy to be managed more effectively as the INR result is independent of the thromboplastin used and therefore comparable across all laboratories.

$$INR = \left(\frac{\text{Patient PT}}{\text{Control PT}}\right)^{ISI}$$

1c. Some people are at particular risk from warfarin therapy

The large number of biological and other variables involved means that achieving good control of INR levels is not a simple task.

- There is no standard response to warfarin - some people are particularly sensitive to the effects of warfarin while others can be relatively resistant.
- Elderly people require lower doses of warfarin to achieve target INRs and may find attending for regular blood tests and adhering to complex warfarin regimens difficult.
- Poor literacy or numeracy skills are associated with poorer control of INR levels.

2. Initiation of warfarin therapy

2a. Initiation protocols

In many cases warfarin is initiated in hospitals because of the presence of active clot formation. In this situation warfarin is started in conjunction with heparin because the anticoagulant effect of warfarin does not occur for approximately five days. Also the initial period of treatment with warfarin may be associated with a procoagulant state; heparin provides some protection from the risks related to this.

For outpatients who do not require rapid anticoagulation, for example, patients with stable atrial fibrillation, a low-dose warfarin initiation protocol can be used (NZGG, 2005). Low-dose initiation is safe, achieves therapeutic anticoagulation in the majority of patients within 3 to 4 weeks and reduces the risk of over-anticoagulation. This is particularly useful for elderly patients.

A number of low-dose protocols are available and there is no evidence to favour one over another. However, it is recommended that to avoid confusion all practice members use the same initiation protocol in most circumstances.

The following protocol uses 3 mg daily doses and requires only weekly INR testing. The majority of patients reach a stable dose within one month and in the trial no patient suffered a thrombotic or bleeding complication in the first month (Janes, 2004). An even more cautious approach is needed for patients on amiodarone or other potentiators of warfarin action (appendix 3) and for people with co-morbidities.

The procoagulant state

The anticoagulant effect of warfarin is attained by blocking the activation of the clotting factors VII, IX, X, and II. However, warfarin also has a simultaneous procoagulant effect, caused by blocking the activation of two endogenous anticoagulants, protein C and protein S. Protein C has a short half-life, therefore it is depleted quickly after the initiation of warfarin therapy. Because both proteins C and S are anticoagulants, a rapid depletion of these proteins leads to a transient hypercoagulable state in the first one to two days of warfarin therapy. The use of high loading doses may potentiate this phenomenon.

Vitamin K - dependent clotting factors		
Name	Function	Half-life
Protein C	Anticoagulant	8 hours
Protein S	Anticoagulant	30 hours
Factor VII	Procoagulant	7 hours
Factor IX	Procoagulant	24 hours
Factor X	Procoagulant	36 hours
Factor II	Procoagulant	50 hours

Regal, 2004

A Low Dose Warfarin Initiation protocol

The guide is only valid if the patient has taken seven days of warfarin before the day 8 INR. If doses have been omitted or the INR is performed early the dose may be seriously overestimated. Due to the high number of biological and other variables inherent in warfarin therapy its use should be augmented by sound clinical judgement.

A low dose protocol for warfarin initiation (Janes, 2004)			
	INR	Warfarin Daily Dose	Notes
Day 1	Obtain Baseline INR	3 mg	
Day 2 - 7		3 mg	
Day 8	< 1.4	6 mg *	* follow blue guide for 2nd week
	1.4 - 1.5	5 mg	
	1.6 - 1.8	4 mg	
	1.9 - 2.1	3 mg	
	2.2 - 2.5	2.5 mg	
	2.6 - 2.7	2 mg	
	2.8 - 3.0	Omit 1-2 days, reduce to 1 mg	
	> 3.0	**Stop Warfarin**. Check causes, high INR protocol and need for warfarin. Repeat INR in 3-5 days. Restart at 1 mg if indicated.	
Day 15	Most patients will have received stable doses on day 8 and others will only need minor dose adjustments		When INR is stable extend dosing interval and transfer to maintenance guide.

Guide for patients on 6 mg on days 8 to 14			
Day 15	< 1.4		Unusual, check adherence, medication etc. Increase to 10 mg
	1.4 - 1.6	8 mg	
	1.7 - 1.8	7 mg	
	1.9 - 2.4	6 mg	
	2.5 - 2.9	5 mg	
	3.0 - 4.0	4 mg	Consider omitting 1-2 days
	4.1 - 5.0	reduce dose by 1-2 mg	Omit 2 days, check doses taken
	> 5.0		Check high INR protocol. Check doses taken. Omit 3 days and check INR

An outpatient slow loading regimen was assessed in 200 outpatients requiring anticoagulation for atrial fibrillation. Patients were started on 3 mg of warfarin daily for 1 week and subsequent doses determined by weekly INR measurement. 86% of patients had an INR greater than 2 by day 15 and 58% had reached a stable maintenance dose by day 22 and 85% by day 29. The INR on day 8 was predictive of maintenance dose. Only 11 patients had an INR greater than 4 and no patient suffered a thrombotic or bleeding complication in the first month (Janes, 2004).

High Risk

Transfer of care across the primary – secondary interface

Transfer of care from secondary to primary care may be high risk for several reasons:

- Poor communication on discharge may leave the primary care clinician with inadequate information to make safe testing and dose adjustment decisions.
- Patients may be discharged from hospital with tablet strengths, which were used for loading doses but are inappropriate for maintenance therapy.
- Patients often leave hospital with other medications, e.g. antibiotics, which can interact with warfarin.
- The maintenance dose is usually much lower then the loading dose given in hospital, and warfarin has a very long half-life, so accumulates leading to over-anticoagulation.

Some New Zealand hospitals have developed protocols for the timely transfer of information about warfarin therapy to primary care on patient discharge. Essential details have been found to be:

- Condition for which warfarin has been prescribed
- Target INR range
- Planned duration of treatment
- Brand and strength of warfarin tablets given
- Last three doses
- Last three INRs
- Date next INR test due

This information can also be usefully placed in the patient-held anticoagulation record ("The Red book").

New Zealand hospitals use a variety of warfarin initiation protocols and there is little evidence that one is any better than another. It is probably wise to follow on with the protocol initiated by their local hospital for patients who start warfarin in the hospital environment. This requires primary care clinicians to have copies of local hospital protocols.

2b. Pre initiation tests

Before starting warfarin a baseline INR/PR should be performed together with an APTT, FBC to exclude thrombocytopenia, and liver function tests.

2c. Detailing the plan for anticoagulation therapy in clinical records

Misunderstandings are less likely when standardised methods are used to record the management plan for anticoagulation therapy in the clinical notes. The method chosen will depend on how clinical records are managed locally but there should at least be a standard location within the patient notes for the following information:

- The patient is on warfarin
- Condition for which prescribed
- Target INR range
- Planned duration of treatment
- Brand of warfarin

The information that a patient is on warfarin must be immediately obvious to any clinician who accesses the patient's clinical record. The prescribing alerts on computer systems cannot be relied on because they are often ignored or turned off.

To create an alert, in MedTech, which opens whenever someone accesses the clinical records of someone on warfarin, see appendix 4.

2d. Target INR range

In most situations the INR target range is 2.0 – 3.0. This range is appropriate for the prophylaxis or treatment of venous thromobo-embolism and reduction of the risk of systemic embolism for people with atrial fibrillation, valvular heart disease or following MI (Campbell, 2001). In some situations higher ranges are more appropriate.

In most situations the target INR range is 2.0 – 3.0.

2e. Prescribing warfarin

- ✓ All clinicians caring for an individual should use the same brand of warfarin
- ✓ Marevan® and Coumarin® are available in New Zealand
- ✓ Marevan accounts for approximately 95% of prescriptions of warfarin in New Zealand
- ✓ The brands are not interchangeable and come in different tablet strengths
- ✓ During community initiation only 1 mg tablets should be used to minimise confusion

2f. Prescribers can use drug labelling to highlight the importance of INR monitoring

The labelling on warfarin medication gives an opportunity to remind patients of the need for regular blood tests. Labels such as "PRN" or "as required" can lead to misunderstandings. A better option may be "Take the dose advised by your doctor or nurse. You need regular INR blood tests to make sure this dose is right for you."

2g. Patient Education

Patients who are well informed and understand what they are doing are more likely to benefit from treatment; therefore effective patient education is an important component of achieving good INR levels.

Patient education needs to cover at least the following key points:

- ✓ Need for patient to regularly remind their doctor, pharmacist, dentist or other health professional they are receiving warfarin
- ✓ Requirement for regular blood tests
- ✓ Adherence to dosage changes following blood test results
- ✓ Importance of avoiding other medications (including herbal medicines and supplements) except following discussion with clinician, pharmacist or other healthcare provider
- ✓ Significance of illness, such as diarrhoea, infection or fever on warfarin use
- ✓ Ability to recognise the signs of possible bleeding

Bleeding is the most serious potential side effect of warfarin.
If patients experience any of the following symptoms, they must call their doctor immediately:

- Red or dark brown urine
- Red or black stool
- Severe headache
- Unusual weakness
- Excessive menstrual bleeding
- Prolonged bleeding from gums or nose
- Dizziness, trouble breathing or chest pain
- Unusual pain, swelling or bruising
- Dark, purplish or mottled fingers or toes
- Vomiting or coughing up blood

The patient-held record traditionally known as "the red book" facilitates patient education and sharing of information between patients and their clinicians about an individual's warfarin therapy and INR monitoring.

Patients should always show their red book when they see a clinician or pharmacist, and when they purchase over-the-counter or alternative medicines. Clinicians and pharmacists can encourage this by asking to see the patient-held record whenever they consult with someone they know to be on warfarin.

Patients and health professionals have a joint responsibility to make sure the record is kept up to date.

3. Monitoring INR

3a. INR testing schedule

Regular testing of INR levels is essential for all people taking warfarin. The first three months have the highest rate of major bleeding (approximately 2%). The rate falls significantly after this. For most people once the INR is stable the rate of INR testing can be extended to two weekly and then 4 to 6 weekly. However people with higher levels of risk, may need more frequent testing.

- The INR is generally considered stable when two or more consecutive tests, performed at least 24 hours apart are within the target range.
- Some fluctuation of the INR within the target range is to be expected and adjustment of the dose is not required. Wide variations within the range over a few days may be more significant (BC Health Services, 2004).

A reasonable standard for good control of warfarin therapy is an INR within the target range 60% of the time (Machin, 2002).

Comments from our UK reviewer: "We have shown INR interval can be extended out to 14 weeks in stable patients. Certainly lots of our patients are at 8-12 weeks". S Janes. (Lidstone, 2000)

For patients initiated with low-dose protocol (warfarin initial dose 2 – 3mg daily):

Initially	**When INR < 4:** Weekly **When INR > 4:** Every 2-3 days	Until stable for 2 consecutive tests
Then:	Fortnightly	Until stable for 2 - 3 consecutive tests
Maintenance:	Most patients can be extended to 4 - 6 weekly testing however a minority may require more frequent testing.	

(Adapted from Janes, 2004)

For patients initiated with higher doses:

Initially	daily for at least five days	Until stable for 2 consecutive tests
Then:	every 3 - 5 days	Until stable for 2 consecutive tests
Then:	weekly	Until stable for 2 - 3 consecutive tests
Then:	fortnightly	Until stable for 2 - 3 consecutive tests
Maintenance:	Most patients can be extended to 4-6 weekly testing however a minority may require more frequent testing	

(Adapted from Horton, 1999)

3b Changes in INR levels

Changes in the INR level in a usually stable patient may be due to a number of reasons:

- Non adherence to dosage regimen
- Drug interactions (pharmaceutical or herbal)
- Major changes in diet or alcohol intake
- Systemic or concurrent disease
- Unknown causes

Non adherence to dosage regimen

An erratic INR may reflect non-adherence to the drug regimen often due to misunderstandings of dosage requirements. A missed dose of warfarin is usually reflected in the INR result 2 to 5 days after the missed dose (Jaffer, 2003), although a response may be seen within 16 hours (National Guideline Clearinghouse, 2006).

Drug interactions

Almost any drug can interact with warfarin; effects are more marked when starting, changing or stopping the dose.

For short courses of a new drug therapy, dose adjustment is not essential. If a known potentiator is prescribed (appendix 3), a slight dose reduction or omission of one warfarin dose may be recommended.

Check INR one week after commencement of a new medication.

If medication is taken for more than five days, check INR one week after commencement. Similar precautions need to be taken when discontinuing or changing doses of a medication. Information on warfarin drug interactions can be found in resources such as your practice management system, MIMs and BNF.

The use of herbal medicines is gaining in popularity, and the number of studies performed on the interactions with warfarin is rather limited. Therefore, it is prudent to assume any herbal medication may have the potential to alter the INR.

Diet

Patients on warfarin are usually advised to consume a reasonably consistent proportion of vitamin K rich foods. This is probably most relevant in patients who have had markedly reduced food intake because of illness, hospitalisation, travel and fad diets (Campbell, 2001). A recent study suggests that the role of excessive dietary vitamin K may have been overstated, with the exception of natto (Japanese fermented soybean) which causes a marked and prolonged inhibition of warfarin (Schurgers, 2004).

Systemic or concurrent disease

Many systemic diseases can influence INR results:

- *Congestive heart failure:* may cause hepatic congestion of blood flow and inhibit warfarin metabolism, this may be particularly troublesome during exacerbations of heart failure.
- *Hypothyroidism:* decreased catabolism of vitamin K clotting factors may decrease INR values.
- *Hyperthyroidism:* conversely, hyperthyroidism may increase catabolism of vitamin K clotting factors and increase INR values.
- *Liver failure:* may cause elevation of INR due to reduced production of clotting factors.
- *Other illnesses:* other intermittent conditions such as fever, vomiting and diarrhoea may affect the INR; ill patients may also reduce their usual dietary intake.

Unknown causes

In many cases, no explanation may be found for unstable INR values. It may be worthwhile discussing aspects of the dosing regimen. Changes in the INR may also be the result of occult causes, such as undisclosed drug use, lifestyle and medical causes.

3c. Managing alterations in the INR

Use a standard guide to assist dose modification

If the fluctuation is minor, changes in weekly doses are usually not required, but a cause should be sought. For more significant fluctuations use of a standard guide reduces the risk of confusion.

There are many guides on dosage adjustment for people on warfarin therapy; there is no evidence to favour one over another. A guide from the British Columbia Health Service is reproduced below.

Dosage Adjustments for Patients on Warfarin Maintenance Therapy, Target 2.0 - 3.0	
INR	Dosage Adjustment
< 1.5	Increase weekly dose by 20% and give one time top-up additional amount equal to 20% of weekly dose
1.5 - 1.9	Increase weekly dose by 10%
2.0 - 3.0	No change
3.1 - 3.9	No change - recheck in one week. If persistent, decrease weekly dose by 10-20%
4.0 - 5.0	Omit 1 dose; decrease weekly dose by 10-20% and recheck in 2-5 days
> 5.0	See guide for Treatment of Patients Overanticoagulated with Warfarin (see section 3d)

- Changes in warfarin dosage may take several days to affect INR. Hence, frequent dosage adjustment (<4-5 days interval) is not recommended.
- Adjustments may need to be modified in the presence of intercurrent illness.

3d. What to do when the INR is high (BC Health Services)

Guideline for Over Anticoagulation	
Clinical	Guideline
INR 5 - 8 without bleeding	1. Stop warfarin 2. Test INR daily until stable 3. Restart in reduced dose when INR < 5 4. Give vitamin K 0.5 - 1 mg oral/sc, if INR fails to fall, or if there is high risk of serious bleeding
INR > 8 with minor bleeding	5. Stop warfarin 6. Consider admission if clinically appropriate 7. Test INR daily until stable 8. Restart in reduced dose when INR < 5 9. Give Vitamin K 1-2 mg oral/sc
High INR and major bleeding	10. Stop warfarin 11. Give Vitamin K 10 mg sc 12. Admit stat

3e. Taking a sample for INR testing

There are no special requirements for the patient prior to collection of blood for INR testing. There is no particular time at which INRs should be collected, but often a time will be recommended that fits into the practice routine. Having the specimen collected on the same day of the week may help with continuity of care as the same practice staff are likely to be on duty.

Blood specimens for INR should be collected into a tube (usually light blue top) containing sodium citrate. The ratio of blood to anticoagulant is important therefore the tube must be filled to the fill mark on the tube.

At the time of collection it is good practice to view the patient handbook, and use this as an opportunity to ask questions specific to the patient's warfarin control.

3f. Questions for the patient when sample taking

Some practices may elect to take blood for INR testing at the surgery rather than sending patients to the laboratory. This gives an opportunity for ongoing patient education and information sharing. Practice nurses have told us they usually discuss adherence to the dosing regimen, changes to medication, major changes in diet and signs of bleeding. They always sight the patient-held record and make sure it is up to date.

As a result of this discussion with the patient any additional notes can be added to the laboratory form. Significant notes may include changes in warfarin dose, or significant changes in diet or addition of new medications.

4. Other issues for INR management

4a. Ceasing warfarin therapy

Warfarin therapy can be discontinued abruptly when the duration of treatment is completed. Prospective studies have not indicated a rebound prothrombotic state and there is no need for gradual withdrawal.

4b. Dental extractions and preoperative warfarin doses

For minor surgical procedures, the warfarin dose should be stopped or adjusted to achieve a target INR of approximately 2.0 on the day of surgery. For major surgery, warfarin should be stopped at least three days prior to surgery; further actions will depend on resulting INR levels and the thrombotic risk of the condition for which the patient is receiving anticoagulation.

Anticoagulation does not need to be stopped for dental extraction for patients with an INR less than 3.0.

4c. Warfarin should be avoided in pregnancy

Pregnant women should never take warfarin, as it is teratogenic (Medsafe, 2002). Women of child-bearing age on warfarin should be using effective contraception and contact their doctor urgently (by six weeks) if they think they are pregnant.

4d. Standardised procedures for rest homes

The establishment of a systematic approach to the use of warfarin is particularly important in rest homes. There are often several health professionals involved in the prescribing, dose adjustment and administration of warfarin. It is essential that there are robust systems in place to guide the processes.

Clear written instructions are necessary to guide rest home staff. Verbal instructions on warfarin therapy in rest homes, for example on changing doses, are fraught with risk and should be avoided whenever possible.

4e. Near patient testing

Near patient testing of INR levels is effective for selected patients. There are risks if patients are not well motivated, or do not fully understand the process, or if quality assurance procedures are not of a high standard.

If you would like to check your current system for maintenance of INR levels you could use bpac's audit, 'Practice audit of the systematic management of INR levels', which has been sent to every practice and is available from www.bpac.org.nz

Guide for using INR to manage warfarin

bpac nz
better medicine

A low dose protocol for warfarin initiation (Janes, 2004)			
	INR	Warfarin Daily Dose	Notes
Day 1	Obtain Baseline INR	3 mg	
Day 2 - 7		3 mg	
Day 8	< 1.4	6 mg *	* follow blue guide for 2nd week
	1.4 - 1.5	5 mg	
	1.6 - 1.8	4 mg	
	1.9 - 2.1	3 mg	
	2.2 - 2.5	2.5 mg	
	2.6 - 2.7	2 mg	
	2.8 - 3.0	Omit 1-2 days, reduce to 1 mg	
	> 3.0	**Stop Warfarin**. Check causes, high INR protocol and need for warfarin. Repeat INR in 3-5 days. Restart at 1 mg if indicated.	
Day 15	Most patients will have received stable doses on day 8 and others will only need minor dose adjustments		When INR is stable extend dosing interval and transfer to maintenance guide.

Guide for patients on 6 mg on days 8 to 14			
Day 15	< 1.4		Unusual, check adherence medication etc. Increase to 10mg
	1.4 - 1.6	8 mg	
	1.7 - 1.8	7 mg	
	1.9 - 2.4	6 mg	
	2.5 - 2.9	5 mg	
	3.0 - 4.0	4 mg	Consider omitting 1-2 days
	4.1 - 5.0	reduce dose by 1-2 mg	Omit 2 days, check doses taken
	> 5.0		Check high INR protocol. Check doses taken. Omit 3 days and check INR

Guideline for Over Anticoagulation

INR 5 - 8 without bleeding

1. Stop warfarin
2. Test INR daily until stable
3. Restart in reduced dose when INR < 5
4. Give vitamin K 0.5 - 1 mg oral/sc if INR fails to fall, or if there is high risk of serious bleeding

INR > 8 with minor bleeding

5. Stop warfarin
6. Consider admission if clinically appropriate
7. Test INR daily until stable
8. Restart in reduced dose when INR < 5
9. Give Vitamin K 1-2 mg oral/sc

High INR and major bleeding

10. Stop warfarin
11. Give Vitamin K 10 mg sc
12. Admit stat

The guide is only valid if the patient has taken seven days of warfarin before the day 8 INR. If doses have been omitted or the INR is performed early the dose may be seriously overestimated. Due to the high number of biological and other variables inherent in warfarin therapy its use should be augmented by sound clinical judgement.

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3.1 - 3.9	No change - recheck in one week. If persistent, decrease weekly dose by 10-20%
4.0 - 5.0	Omit 1 dose; decrease weekly dose by 10-20% and recheck in 2-5 days
> 5.0	See guide for Treatment of Patients Overanticoagulated with Warfarin (see section 3d)

Treatment Guide for managing Warfarin

INR testing frequency

- The INR is generally considered stable when two or more consecutive tests, performed at least 24 hours apart are within the target range
- Some fluctuation of the INR within the target range is to be expected and adjustment of the dose is not required but wide variations within the range over a few days may be more significant.

For patients initiated with low-dose protocol (warfarin initial dose 2 -3 mg):		
Initially	**When INR < 4:** Weekly **When INR > 4:** Every 2-3 days	Until stable for 2 consecutive tests
Then:	Fortnightly	Until stable for 2 consecutive tests
Maintenance:	Most patients can be extended to 4-6 weekly testing however a minority may require more frequent testing	

For patients initiated with higher doses:		
Initially	Daily for at least five days	Until stable for 2 consecutive tests
Then:	every 3 - 5 days	Until stable for 2 consecutive tests
Then:	weekly	Until stable for 2 - 3 consecutive tests
Then:	fortnightly	Until stable for 2 - 3 consecutive tests
Maintenance:	Most patients can be extended to 4-6 weekly testing however a minority may require more frequent testing	

Patient education needs to cover at least the following key points:

- ✓ Need for patient to regularly remind their doctor, pharmacist, dentist or other health professional they are receiving warfarin
- ✓ Requirement for regular blood tests
- ✓ Adherence to dosage changes following blood test results
- ✓ Importance of avoiding other medications (including herbal medicines and supplements) except following discussion with clinician, pharmacist or other healthcare provider
- ✓ Significance of illness, such as diarrhoea, infection or fever on warfarin use
- ✓ Ability to recognise the signs of possible bleeding

Specimen Collection:

- Blood specimens should be collected into a light blue top tube
- The tube must be filled completely
- View the patient handbook
- Ask questions specific to warfarin control, for example:
  - Adherence to the dosing regimen
  - Any changes in diet
  - Any medications the patients may have stopped or started
  - Signs of bleeding

Bleeding is the most serious potential side effect of warfarin.
If patients experience any of the following symptoms, they must call their doctor immediately:

Red or dark brown urine	Excessive menstrual bleeding	Unusual pain, swelling or bruising
Red or black stool	Prolonged bleeding from gums or nose	Dark, purplish or mottled fingers or toes
Unusual weakness, Severe headache	Dizziness, trouble breathing or chest pain	Vomiting or coughing up blood

Appendix 3 Drugs which potentiate the action of warfarin

Drugs which potentiate the action of warfarin					
Antibiotics	**Anti-inflammatory**	**Cardiac**	**Gastrointestinal**	**Psychiatric**	**Other**
Cotrimoxazole	NSAIDs	Amiodarone	Omeprazole	Paroxetine	Tramadol
Erythromycin	COX II inhibitors	Propranolol	Cimetidine	Fluoxetine	Phenytoin
Norfloxacin	Sulfinpyrazone	Clofibrate		Citalopram	Tamoxifen
Roxsithromycin	Salicylates				
Cephalosporin	Paracetamol				
Ciprofloxacin					
Azithromycin					
Fluconazole					
Miconazole (including gel)					
Metronidazole					
Isoniazid					

Appendix 4. Adding an alert for patients on warfarin

An alert which appears whenever the clinical records of a patient on warfarin are accessed. For use with MedTech.

To set up an alert to use for patients on warfarin

1. From the menu select: Setup > Patient Register > Alert
2. Put a code, perhaps “warf”, in the appropriate box and put “On Warfarin” in the description box.
3. Click OK, your alert is now set up for use.

To use the warfarin alert for a particular patient

1. When the patient’s clinical records are open
2. From the menu select: Module > Alerts
3. Click on the box in the window that opens to assign a new alert to the patient
4. In the code box enter “warf” or whatever code you used.
5. In the text box underneath put details of:
    - Condition for which patient is on warfarin
    - Date therapy started
    - Planned duration of treatment
    - Target INR

Note: you cannot use the enter key when you are in this text box.

6. Tick the box labelled Auto Prompt Alert
7. Click OK, your alert should now open whenever the patient’s clinical records are accessed.

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