GUIDELINES & PROTOCOLS
ADVISORY COMMITTEE
SUMMARY OF GUIDELINE

Effective Date: October 1, 2010

Warfarin Therapy Management in Adults

For full Guideline please go to website: www.BCGuidelines.ca

Warfarin is increasingly used due to population aging and the drug's beneficial effect in atrial fibrillation; however, over 50% of patients on warfarin are managed suboptimally and many who would benefit from the drug do not receive it.

A. INITIATION OF WARFARIN THERAPY

1. **Contraindications** (for a complete list, refer to the product monograph):

Absolute Contraindications	Some Relative Contraindications
- Severe or active bleeding diathesis - Non-adherence to medication and INR monitoring - Pregnancy (especially first trimester & 2-4 weeks pre-delivery) - Allergy or intolerance to warfarin (alternative is nicoumalone)	- Uncontrolled hypertension >180/100 mm Hg - Severe liver disease - Recent surgery and procedures involving the nervous system, spine, or eye

2. **Establish baseline INR:** Should be done in every case, and will guide further therapy.

3. **Initial warfarin dose:**
   - 5 mg/day for most patients; start lower for: age > 70; baseline INR > 1.1; hypoalbuminemia, e.g., malnourished, liver disorders, post-operative; impaired nutrition (weight < 45 kg); heart failure; known to take medications that increase sensitivity to warfarin; or documented history of sensitivity to warfarin.
   - Whenever feasible, prescribe a single strength tablet (e.g., 1 mg) so doses are multiples.
   - Warfarin should be taken once a day at the same time in the evening with INR testing in the morning.

B. INR TARGET AND FREQUENCY OF MONITORING

1. **Optimal maintenance dose and target INR**
   - Optimal maintenance dose varies from patient to patient and at different times in the same patient.
   - Two therapeutic ranges for target INR, depending on indication:
     - Most indications: INR 2.5 (range 2.0-3.0)
     - Some heart valves: INR 3.0 (range 2.5-3.5) for mechanical heart valves in mitral position and non-bileaflet valves in aortic position (establish desired range with a specialist physician).

2. **Monitoring (also see Figure 1 on the reverse)**
   - Need close monitoring long term due to warfarin's narrow therapeutic index and a high risk/benefit ratio.
   - Frequent changes are not recommended because INR may not change for 4-5 days after a dose change, and INR rises initially without concomitant clinical anticoagulant effect.
   - Initially monitor INR q 2-4 days (daily if on therapeutic heparin) until target range for 2 consecutive values.
   - Once INR has stabilised it can be monitored weekly, then q4 weeks.
   - Increase frequency of INR testing (to q 2-4 days) if: non-therapeutic INR, intercurrent illness, any medication change (including herbal), or significant diet change.

C. MAINTENANCE THERAPY, INCLUDING DOSAGE ADJUSTMENTS (also see Table 1 on the reverse)

- Do not adjust drug dose for minor INR fluctuations within the target range.
- Contact the patient directly for fluctuations outside the target range to determine a cause, e.g., changes in drug dosage, compliance, medications including OTCs, diet, alcohol, and illness.
- The recent trend is to change the total weekly warfarin dose (TWD), e.g., if the patient is taking 5mg/day, the weekly dose is 35mg. If the dose must be decreased by 10%, then the weekly dose should be 35mg - 3.5mg = 31.5mg and the daily dose becomes 31.5mg / 7 = 4.5mg.

D. RISK FACTORS FOR BLEEDING COMPLICATIONS

- Age > 70 years; within first year of warfarin treatment.
- Clinical conditions: uncontrolled hypertension; heart failure; history of GI haemorrhage; active peptic ulcer; hepatic insufficiency; thrombocytopenia; platelet dysfunction; coagulation defect; underlying malignancy; history of stroke, cognitive or psychological impairment; and renal insufficiency.
- Other: Recent trauma, history of falls, excessive alcohol, use of ASA or NSAIDs, discontinuing medications that reduce INR.

Figure 1: Recommended Frequency of INR Monitoring

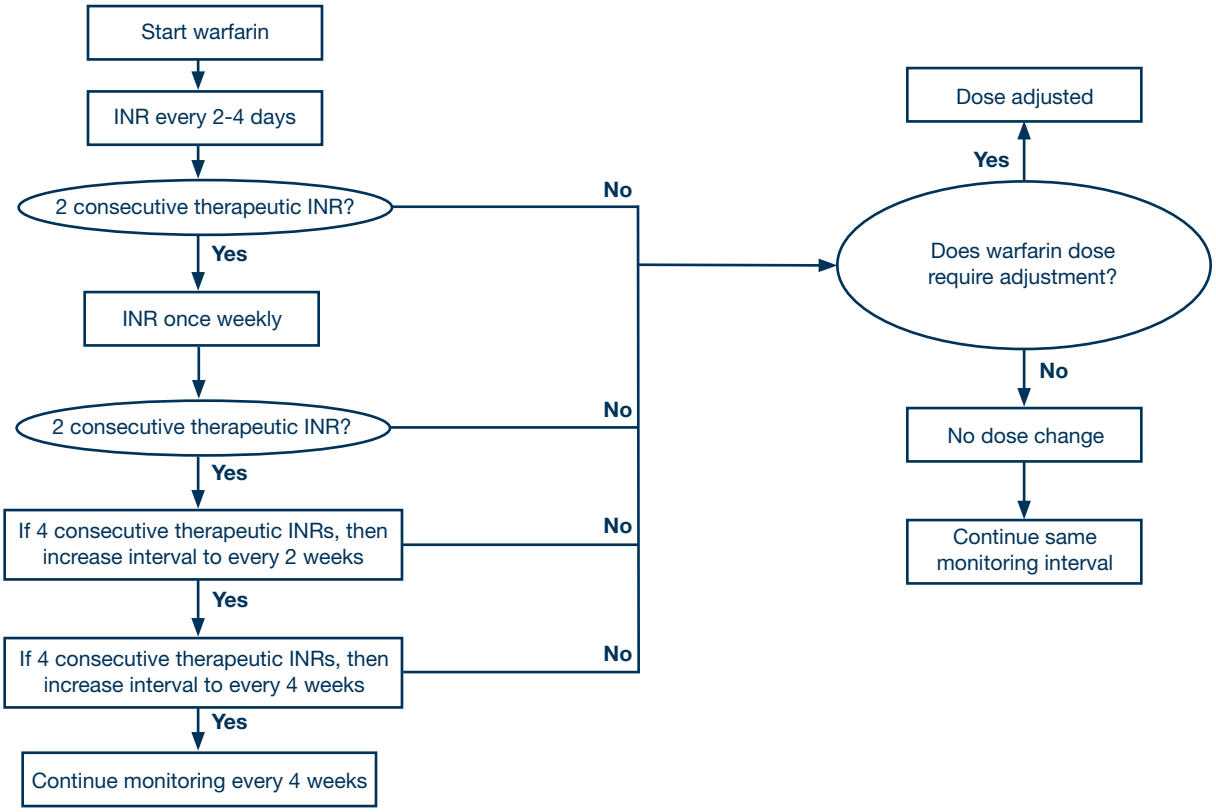

Table 1: Warfarin Dosage Adjustments (Target INR 2.0 - 3.0 or 2.5 - 3.5, No Significant Bleeding)

INR	Intervention
≤ 1.5	- Give one time top-up equal to 20% of weekly dose and increase weekly dose by 10-20%
1.5 < INR < therapeutic range	- No change in dose - If two consecutive INRs are low, increase weekly dose by 10-20%
INR in therapeutic range	- No change
INR > therapeutic range but < 5.0	- Lower weekly dose (10-20%) or consider omitting one single dose - Increase the frequency of INR monitoring and resume therapy at 10-20% lower weekly dose when INR therapeutic - Note: If the INR is only minimally elevated (0.1 - 0.4 above upper limit of the therapeutic range), dose reduction may not be necessary[14]
INR 5.0 – 9.0*	- Omit 1 to 2 doses then recheck INR - Increase the frequency of INR monitoring and resume therapy at 10-20% lower weekly dose when INR therapeutic - If the patient is at high risk of serious bleeding, consider administering vitamin K** 1 to 2 mg orally
>9.0; no bleeding	- Discontinue warfarin temporarily, consider administering vitamin K 2-5 mg orally then recheck INR*** - Increase the frequency of INR monitoring and resume therapy at 20% lower weekly dose when INR therapeutic - Give additional vitamin K if INR is not substantially reduced by 24 hrs***
KEY: PO = orally; TR = therapeutic range; TWD = total weekly warfarin dose	

TABLE 1 NOTES:

* Bleeding risk increases exponentially from INR 5.0 to 9.0 and should be monitored closely.
** If vitamin K is not available in your local pharmacy, it can be obtained from your local ER. (avoid IM injections)
*** The effect of a single dose of vitamin K on the INR can be expected between 8-24 hours.