

FAST FACTS AND CONCEPTS #278 WARFARIN AND PALLIATIVE CARE

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Background The number of patients with advanced disease taking warfarin (Coumadin) and receiving specialist palliative care or admitted to hospice care is increasing due to the increased indications for anticoagulation. For many patients, the goals of anticoagulation include preventing embolic stroke due to dilated cardiomyopathy, atrial fibrillation, or prosthetic valves, until close to the time of death (see *Fast Fact* #236 for information on venothromboembolism). Most medical literature and on-line calculators deal with starting warfarin. None address the management of patients with advanced disease. This *Fast Fact* reflects expert opinion on managing warfarin near the end-of-life.

Physiology Vitamin K is an important cofactor in the hepatic synthesis of coagulation proteins. Warfarin inhibits vitamin K epoxide reductase, effectively reducing the amount of active vitamin K in the body. The principle source of vitamin K is ingested food, particularly leafy greens, which is acted upon by intestinal bacteria. Patients who are not eating well absorb less vitamin K and will have a higher INR so will need less warfarin to maintain the same anticoagulant effect. Antibiotics and liver synthetic failure will also raise the INR requiring warfarin dose reduction. Therefore, monitoring the INR is required for patients taking warfarin to prevent an increased risk of bleeding (GI bleed and hemorrhagic stroke).

Measurement of Effect An INR (International Normalized Ratio) of 2-3 is the therapeutic range for most patients. This is a standardized measure of clotting that reflects the sum total of all of the clotting factors that are dependent on Vitamin K: II, VII, IX and X as well as the anticoagulant proteins C and S. The long half-life of about 50 hours (2 days) of prothrombin (Factor II) synthesized by the liver means the antithrombotic effect of a changed warfarin dose is *not approached until 3 half-lives (5-6 days)*.

Common Error When informed of an INR that is too high or too low, the less informed clinician will change the daily dose of warfarin and ask for a repeat value for the INR in 1 or 2 days. If it is too high or too low, the dose is changed again. Since steady state is not reached before the change, a see-saw of increasing and decreasing doses and repeated measurements is a burden to patients and health care professionals and puts the patient at risk from an INR that veers wildly from subtherapeutic to supratherapeutic levels.

Guidance for Management of Warfarin Dosing in Advanced Disease (based on expert opinion)	
If the INR is low (< 1.5) and appetite same	Increase dose by 20% and recheck in 1 week
If the INR is low (< 1.5) and appetite is worse	Leave dose unchanged and recheck in 1 week
If the INR is between 1.5 and 3.5	Leave dose unchanged
If the INR is high (> 3.5 but < 8) and appetite same	Hold one dose and resume at 20% decreased dose
If the INR is high (> 3.5 but < 8) and appetite worse	Hold one dose and resume at 50% decreased dose
If the INR is very high (> 8)	Hold warfarin and repeat INR in 1 week
If the INR is high and there is bleeding	One dose oral vitamin K; emergent care may be indicated based on severity of the bleeding and patient's goals of care
If the INR is stable and patient stable	Check INR monthly

When to Stop This is a challenging clinical decision. The management of the INR by pharmacists in many settings makes it even more difficult to keep the risks/benefits of warfarin therapy balanced with the clinical assessment of the patient at home.

- Most experts would agree that the risk of intracranial hemorrhage for a patient taking warfarin who insists on being ambulatory but wobbly enough to fall is greater than the benefit of preventing embolic stroke.
- Similarly, when dietary intake drops 50% or more from a usual balanced diet (especially when intake is only favorites like ice cream and not vitamin K rich foods) or when eating is highly erratic, the risk of bleeding escalates exponentially if warfarin dosing continues.
- No warfarin should be given to the patient who develops liver failure.
- The patient who does not agree to checking an INR should stop taking warfarin.
- Finally, all would agree that warfarin therapy should stop when there is frank bleeding.

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