

Guidelines for the Management of a Supratherapeutic INR or Acute Bleeding Episode Associated with Warfarin Use

Condition*	Recommendation
INR above therapeutic range but <4.5 No evidence of bleeding	<ol style="list-style-type: none"> 1. Lower warfarin dose or omit dose. 2. Monitor INR more frequently. 3. Resume at lower dose when INR therapeutic. 4. If only minimally above therapeutic range, no dose reduction may be required.
INR between 4.5 and 10 No evidence of bleeding	<ol style="list-style-type: none"> 1. Omit next one or two doses of warfarin. 2. Monitor INR more frequently. 3. Resume warfarin at an appropriately adjusted dose when INR therapeutic. <p style="text-align: center;">----- OR -----</p> <ol style="list-style-type: none"> 1. Omit warfarin dose. 2. Give vitamin K 1.25-2.5mg orally if patient at increased risk of bleeding. 3. May repeat vitamin K 1.25-2.5mg orally if INR still high after 24 hours. 4. Resume warfarin at an appropriately adjusted dose when INR therapeutic.
INR >10 No evidence of bleeding	<ol style="list-style-type: none"> 1. Hold warfarin 2. Give vitamin K 2.5 orally (expect substantial reduction in INR in 24-48 hours) 3. Monitor INR more frequently. 4. May repeat vitamin K in 24 hours if necessary. 5. Resume warfarin at an appropriately adjusted dose when INR therapeutic.
‡ Moderate to significant bleeding at any elevation of INR, unlikely to decompensate	<ol style="list-style-type: none"> 1. Hold warfarin 2. Give vitamin K 5-10mg by slow IV infusion. 3. May supplement with fresh frozen plasma, depending on the urgency of the situation. 4. Vitamin K may be repeated every 12h
‡ Serious bleeding at any elevation of INR, with risk for hemodynamic instability	<ol style="list-style-type: none"> 1. Hold warfarin 2. Give vitamin K 5-10mg by slow IV infusion. 3. Supplement with fresh frozen plasma. 4. Vitamin K may be repeated every 12h
‡ Major, life-threatening bleeding at any elevation of INR	<ol style="list-style-type: none"> 1. Hold warfarin. 2. Give vitamin K 5-10mg by slow IV infusion. 3. Supplement with prothrombin complex concentrate (KCentra)♦ or fresh frozen plasma. 4. Vitamin K may be repeated every 12h.

Guidelines for Reversal of Warfarin for Invasive Procedures

Reversal for urgent surgical or other invasive procedure	Vitamin K 2.5-5mg orally or IV. May also consider fresh frozen plasma or prothrombin complex concentrate (KCentra)♦ in addition to vitamin K if more immediate reversal is needed.
Reversal in patients who require temporary interruption of warfarin before surgery or a procedure and whose INR is still above goal for procedure one day before procedure	Vitamin K 2.5mg orally

◆ KCentra Dosing:

Pretreatment INR 2 to <4: Give 25 units/kg, with maximum dose of 2,500 units

Pretreatment INR 4 to 6: Give 35 units/kg, with maximum dose of 3,500 units

Pretreatment INR >6: Give 50 units/kg, with maximum dose of 5,000 units

‡ CHEST guidelines recommend use of prothrombin complex concentrate rather than fresh frozen plasma for rapid reversal in patients with major bleeding (Grade 2C). Guidelines also suggest the additional use of vitamin K 5-10mg by slow IV injection rather than reversal with coagulation factors alone (Grade 2C).

* If continuing warfarin therapy is indicated after high doses of vitamin K, heparin or low molecular weight heparin can be given until the effects of vitamin K have been reversed, and the patient becomes responsive to warfarin therapy. It should be noted that INR values > 4.5 are less reliable than values in or near the therapeutic range. Thus, these guidelines represent an approximate guide for elevated INRs.

CHEST guidelines **recommend oral administration of vitamin K rather than subcutaneous or IV** for patients with mild to moderate elevation of INRs without major bleeding. This is a Grade 1A recommendation, the highest rating of trial evidence and expert opinion. Literature shows that oral vitamin K is effective for treatment of warfarin-associated coagulopathy and that subcutaneous vitamin K does not produce reliable, rapid reductions in INR. SQ vitamin K is no longer recommended.

High doses of vitamin K, though effective, may lower the INR more than is necessary and may lead to warfarin resistance for a week or more. While larger doses inhibit the vitamin K cycle for a longer time, eventually lowering the INR more substantially, they do not decrease the INR more quickly. Thus, small doses, and if necessary, repeated small doses, can be better for decreasing INR while preventing warfarin resistance.

Doses of ≤ 5mg vitamin K orally will substantially decrease the INR in 24 hours, and doses > 5-10mg orally will substantially decrease the INR in 24-48 hours. Doses > 10mg may take much longer to achieve full INR lowering and may eliminate warfarin sensitivity.

References

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