Guidelines for Warfarin Reversal with Vitamin K

Reversal of warfarin is complex. Guidelines published in CHEST in 2001 provide greater understanding of how to manage warfarin reversal using vitamin K. Below is a summary of these guidelines.

**Introduction**
When the INR (International Normalized Ratio) is in therapeutic range and therapy is interrupted, the INR will return to normal in 4-5 days. Treatment with vitamin K substantially reduces the INR in 24 hours. Since the absolute bleeding risk is low even in the presence of an excessively prolonged INR, patients may be managed by interruption of warfarin therapy and monitoring frequently, provided the patient is not at high risk of bleeding or already developed bleeding.

**Warfarin Resistance**
When large doses of vitamin K are administered, warfarin resistance may occur for up to a week.

**Routes of Administration**
- **Intravenous:** vitamin K administered by IV injection may be associated with anaphylactic reactions. If IV administration is necessary, the rate of infusion should not exceed 1mg/min.
- **Subcutaneous:** The response to vitamin K administered SQ may be delayed and unpredictable.
- **Oral:** Oral administration is predictably effective, safer and more convenient than parenteral routes and is the treatment of choice. Doses other than the available tablet size of 5mg may be obtained using the parenteral form diluted in a flavored beverage.

**Continued administration**
Since warfarin has a much longer duration of action than vitamin K, vitamin K may need to be re-administered in patients with massive warfarin overdose or ongoing bleeding.
### Guidelines for Warfarin Reversal with Vitamin K Continued

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<th>INR</th>
<th>Management</th>
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| Greater than therapeutic goal but less than 5 (> goal but < 5) No significant bleeding | - Lower dose or omit a dose and resume therapy at lower dose once INR therapeutic.  
- If INR only minimally higher than therapeutic range, no dosage adjustment may be necessary. |
| Greater than 5 but less than 9 (> 5 but < 9) No significant bleeding | - Omit next 1-2 doses, monitor INR more frequently and resume therapy at lower dose once INR therapeutic.  
- If patient at increased risk of bleeding, omit dose and administer vitamin K 1-2.5 mg orally.  
- If rapid reversal necessary (requires urgent surgery), administer vitamin K 2-4mg orally and expect INR reduction within 24h.  
- If INR still high, administer additional vitamin K 1-2mg orally. |
| Greater than 9 (>9) No significant bleeding | - Hold warfarin therapy and administer vitamin K 3-5 mg orally and expect substantial INR reduction in 24-48 hours.  
- Monitor INR more frequently and administer additional vitamin K as needed.  
- Resume therapy at lower dose once INR therapeutic. |
| Greater than 20 (> 20) Serious bleeding | - Hold warfarin therapy and administer vitamin K 10 mg slow IV infusion, supplemented with fresh plasma or prothrombin complex concentrate depending on urgency of the situation.  
- Administration of vitamin K may be repeated every 12 hours. |
| Life-threatening bleeding | - Hold warfarin, administer prothrombin complex concentrate supplemented with vitamin K 10 mg slow IV infusion; repeat as necessary depending on INR. |