

Vitamin K1 (Phytonadione)

Vitamin K1 (phytonadione) reverses anticoagulation from vitamin K antagonists, such as warfarin and long acting anticoagulant rodenticides (LAARs), including brodifacoum, bromadiolone, and diphacinone. With supratherapeutic or toxic doses of warfarin or LAARs, deficiencies in vitamin K occur, resulting in a lack of active vitamin K dependent clotting factors (II, IV, IX, X) and increased risk of severe bleeding events.

Indications/Mechanism: Vitamin K1 is indicated when there is evidence of over-anticoagulation (elevated INR) requiring intervention. Vitamin K1 provides exogenous vitamin K that is reduced to its active hydroquinone form which allows activation of vitamin K dependent clotting factors and reduces the risk of bleeding.

Dosing: The oral route for vitamin K1 administration is preferred. Vitamin K1 may be administered IM, IV, and SC; however, the IV route has been associated with anaphylactoid reactions which can occur rarely with IM and SC routes.

Dosing in adults and in children who require anticoagulation (taken from *Chest* 2012;141(2)(Suppl): e152S-e184S):

- **INR 4.5-10 and no significant bleeding:** Vitamin K1 not indicated. Monitor INR q 12-24 hours.
- **INR >10 with no significant bleeding:** Hold warfarin for several doses and give 2.5 to 5 mg of vitamin K1. If INR is not sufficiently reduced in 24 hrs, use additional vitamin K1 as necessary.
- **Significant bleeding at any INR elevation:** Hold warfarin therapy, and give 5-10 mg vitamin K1 by slow IV infusion, and Kcentra (4 factor prothrombin complex concentrate) or NovoSeven (Coagulation Factor VIIa [Recombinant]). Vitamin K1 can be repeated every 12 hrs.

Dosing in adults and children who ingest warfarin and do not require anticoagulation:

Vitamin K1 at doses of 1 to 5 mg orally (child) or 10 mg orally (adult) is administered until the INR is <2 or close to normal. Vitamin K1 may be used parenterally if there is active bleeding. Single acute ingestions do not commonly result in significant coagulopathies in patients not on chronic warfarin, so prophylactic administration is usually not warranted.

Dosing for long acting anticoagulant rodenticide poisoning:

Vitamin K1 should not be administered prophylactically to asymptomatic patients with LAAR overdose. One or two doses of vitamin K1 will not be effective to treat a coagulopathy that will persist for weeks. It will also cause a delay in the onset of INR abnormality which may

Phytonadione (continued)

impair the clinician's ability to diagnose the problem. Some cases have required doses of 50 to 250 mg of vitamin K1 daily for weeks to months. Initial management of LAAR overdose is similar to warfarin. Patients with significant bleeding should receive vitamin K1 10 mg IV plus fresh frozen plasma or KCentra. Patients without bleeding or with minor bleeding receive 50 mg BID (INR <10) or TID (INR >10). The INR should be monitored daily and dose titrated as needed to achieve control of INR (<2.5). Once control of INR is achieved, INR is followed every 2 weeks until normal. Vitamin K1 dose is adjusted as needed and titrated downward by 10-15% with the interval depending on INR response.

Administration:

Oral vitamin K1 is available as Mephyton® in 5 mg tablets. Although the preferred route is oral, vitamin K1 is also available for IV, IM, and SC administration as AquaMEPHYTON® and vitamin K1 emulsion for injection in 2 mg/mL and 10 mg/mL concentrations. The preparation should be diluted with preservative-free 5% dextrose, 0.9% NaCl, or 5% dextrose in 0.9% NaCl, and administered slowly, at a rate not to exceed 1 mg/min in adults to avoid risk of anaphylactoid reactions. Parenteral administration should be reserved for cases of life-threatening bleeding.

Contraindications: Hypersensitivity to vitamin K1 products

Adverse Effects: Oral vitamin K1 is well-tolerated with no reports of adverse effects except overcorrection of INR. IV and IM vitamin K1 administration have led to anaphylactoid reactions even when diluted and infused slowly.

For more on phytonadione:

- Howland MA. *Antidotes in Depth: Vitamin K1*. In: Hoffman RS, Howland MA, Lewin NA, Nelson LS, Goldfrank LR, editors: *Goldfrank's Toxicologic Emergencies*. 10th ed. New York NY, 2015. p836-838.
- Holbrook A, Schulman S, Witt DM, et al. *Evidence-based management of anticoagulant therapy: antithrombotic therapy and prevention of thrombosis*. American College of CHEST Physicians *Evidence-Based Clinical Practice Guidelines (9th Edition)*. *Chest* 2012;141(2)(Suppl): e152S-e184S.

December 2010 (revised November 2012, February 2013, November 2018)