

# Supporting evidence for warfarin reversal

“There is a close relationship between the INR and risk of bleeding. The risk of bleeding increases noticeably once the INR exceeds 4, and the risk rises sharply with values greater than 5. In addition to stopping warfarin when the effect is excessive, vitamin K<sub>1</sub> can be given, and coagulation factors replaced by infusing a prothrombin complex concentrate (PCC) and fresh frozen plasma (FFP). The choice of approach is based largely on clinical judgement, because no randomised trials have compared these strategies in terms of clinical outcomes”.<sup>1</sup>

These comments above from the “consensus” document reflect most evidence where we can offer relatively clear guidelines along a spectrum commensurate with patient circumstances. The recent update of these guidelines is incorporated into the ECI tables.<sup>6</sup>

Patients with an INR of less than 4.5 and who are not bleeding can be managed at home and that simple withholding of one dose or dose adjustment is sufficient. Although we might repeat the INR daily, it takes 3 or 4 days to see the results of dose adjustment. Watching more closely is required to insure that the value is not trending up.

Patients with an INR of 4.5-10 who are not bleeding and are low risk for bleeding complications may be able to be discharged with close follow-up and a safe discharge environment. Oral vitamin K<sub>1</sub> using the IV formulation at 2 mg is suggested as it will reduce the INR a significant amount in 24 hours but not be enough to interfere with subsequent anticoagulation.<sup>2 3</sup> In those who cannot take oral medications then 1 mg of IV vitamin K<sub>1</sub> will have a similar but slightly faster action. In some papers and guidelines the consensus is not to “routinely” use Vitamin K.<sup>4</sup> We are simply decreasing the INR more rapidly with Vitamin K and at lower doses it appears this confers no ongoing risk of dose adjustment or prothrombotic events. In patients who have minor bleeding not readily controlled by standard measures it may be useful to use Vitamin K. The guidelines will allow a spectrum of use of the various tools.

“It is now clear that oral vitamin K has no therapeutic usefulness in clinical settings that require rapid warfarin reversal because it works too slowly”.<sup>3</sup>

Prothrombinex-VF™ is the only product routinely used in Australia and New Zealand it has low levels of Factor VII, which is provided by the FFP. The dose range 25-50 IU/kg is given but there is some evidence that the lower end of the range may be adequate.<sup>5</sup> There is a graded dose scale now considered depending on current and target INR found in the updated consensus guidelines.<sup>6</sup> Globally, use of Prothrombinex style products alone is proving

adequate, work is ongoing in this area. The most recent updates 2013 <sup>6</sup> recommends using FFP in addition to Prothrombinex where there is life or organ threatening bleeding. See below <sup>7</sup> for frequently asked questions on Prothrombinex.

---

<sup>1</sup> [Warfarin reversal: consensus guidelines, on behalf of the Australasian Society of Thrombosis and Haemostasis.](#) Ross I Baker, Paul B Coughlin, Alex S Gallus, Paul L Harper, Hatem H Salem and Erica M Wood; the Warfarin Reversal Consensus Group *MJA*, 2004; 181 (9): 492-497

<sup>2</sup> [Reversal of excessive effect of regular anticoagulation: low oral dose of phytonadione \(vitamin K1\) compared with warfarin discontinuation.](#) Pengo V, Pansato A, Garelli E, Zasso A, Biasiolo A *Blood Coagulation and fibrinolysis*, 1993 Oct; 4 (5): 739-41

<sup>3</sup> [A comparison of the efficacy and rate of response to oral and intravenous Vitamin K in reversal of over-anticoagulation with warfarin.](#) Watson HG, Baglin T, Laidlaw SL, Makris M, Preston FE. *British Journal of Haematology*, 2001 Oct; 115 (1): 145-9

<sup>4</sup> [Antithrombotic Therapy and Prevention of Thrombosis](#), 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines.

<sup>5</sup> [Prothrombinex use for the reversal of warfarin: is fresh frozen plasma needed?](#) Julie H Crawford and Bradley M Augustson *MJA*, 2006; 184 (7): 365-366

<sup>6</sup> [An update of consensus guidelines for warfarin reversal](#) Tran H, Chunilal S, Harper P, Tran H, Wood E and Gallus A, on behalf of the Australasian Society of Thrombosis and Haemostasis *Med J Aust* 2013; 198 (4): 198-199

<sup>7</sup> [Answers to Frequently Asked Questions \(FAQs\) for PROTHROMBINEX®- VF For Use by the AUSTRALIAN RED CROSS BLOOD SERVICE](#), August 2009