Warfarin reversal

Summary of current update

Following the recent publication in the MJA by The Australasian Society of Thrombosis and Haemostasis (ASTH) there have been some changes made to Warfarin reversal guidelines.

Bleeding complications of warfarin

Bleeding risk is related to age, a prior bleeding history and specific comorbidities. Elderly patients are generally more sensitive to warfarin and need a lower mean daily dose. Changes to or addition of other medications can affect the INR/increase risk of bleeding. Drugs that commonly alter warfarin metabolism include antibiotics, amiodarone, statins, anticonvulsants and herbal medications for example St John's Wort.

Vitamin K

The intravenous route achieves a more rapid response compared with oral administration, with an onset of action seen within 6–8 hours. Both oral and IV routes achieve a similar correction of INR by 24 hours. Vitamin K should not be administered by subcutaneous or intramuscular routes.

Prothrombinex Complex Concentrate (PCC)

PCC is formulated with 3 factors (II, IX and X) or 4 factors (II, VII, IX and X). Prothrombinex-VF is a three-factor PCC. It is the product currently used in Australia. Recommended dosage of prothrombinex in 2005 was 25-50 IU/kg. This has been replaced by titrated dosing according to the initial INR and the target INR.

Fresh Frozen Plasma (FFP)

The new recommendation is that FFP should not be used routinely to reverse warfarin.
FFP should be used with PCC in life-threatening bleeding. Where PCC is unavailable and emergency reversal is required, FFP is to be used with vitamin K.

The main focus of the new guidelines is:

- Warfarin therapy complicated by bleeding
- A supratherapeutic INR with no bleeding
- Warfarin therapy during invasive procedures

The first 2 scenarios are detailed below. The supporting evidence is found in 'An update of consensus guidelines for warfarin reversal'. Huyen A Tran, Sanjeev D Chunilal, Paul L Harper, Huy Tran, Erica M Wood and Alex S Gallus, on behalf of the Australasian Society of Thrombosis and Haemostasis. Med J Aust 2013; 198 (4): 198-199.

Summarised by the ECI from "An update of consensus guidelines for warfarin reversal" Huyen A Tran, Sanjeev D Chunilal Huy Tran Erica M Wood and Alex S Gallus Medical Journal of Australia2013;198(4):198-199

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Management of patients on warfarin therapy with bleeding*

Clinical Setting	Recommendations
INR >1.5 with life threatening/critical organ bleeding	• Cease Warfarin • Vitamin K 5.0-10.0mg IV *and* • Prothrombinex-VF 50IU/kg *and* • Fresh Frozen Plasma 150-300ml • If Prothrombinex unavailable administer FFP 15ml/kg
INR >2 with clinically significant bleeding (not life threatening)	• Cease Warfarin • Vitamin K 5.0-10.0mg IV *and* • Prothrombinex 35-50IU/kg according to INR (separate box) • If Prothrombinex unavailable administer FFP 15ml/kg
Any INR with minor bleeding	• Omit Warfarin, repeat INR the following day and adjust warfarin dose to maintain INR in therapeutic range • If bleeding risk high¶ or INR >4 consider Vitamin K orally 1.0-2.0mg or 0.5-1.0mg IV

INR=international normalised ratio IV=intravenously

* Indication for warfarin therapy should be reviewed; if clinically appropriate, consider permanent cessation.

¶ Recent major bleed (within previous 4 weeks) or major surgery (within previous 2 weeks), thrombocytopenia (platelet count, < 50□109/L), known liver disease or concurrent antiplatelet therapy.

Prothrombinex Dosing

	Initial INR			
Target INR	**1.5-2.5**	**2.6-3.5**	**3.6-10**	**>10**
0.9-1.3	30IU/kg	35IU/kg	50IU/kg	50IU/kg
1.4-2.0	15IU/kg	25IU/kg	30IU/kg	40IU/kg

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Management of patients on warfarin therapy with high INR and no bleeding

Clinical Setting	Recommendations
INR higher than the therapeutic range but <4.5 and no bleeding	• Lower or omit the next dose of warfarin • Resume therapy at a lower warfarin dose when the INR approaches therapeutic range • If the INR is only minimally above therapeutic range (up to 10%) dose reduction is generally not necessary
INR 4.5–10.0 and no bleeding	• Cease warfarin therapy; consider reasons for elevated INR and patient-specific factors. Vitamin K1 is usually unnecessary • If bleeding risk is high¶ consider vitamin K 1.0–2.0mg orally or 0.5–1.0mg IV • Measure INR within 24 h • Resume warfarin at a reduced dose once INR approaches therapeutic range
INR>10.0 and no bleeding	• Cease warfarin therapy, administer 3.0–5.0mg vitamin K orally or IV • Measure INR in 12–24 h. Close monitoring of INR daily to second daily over the following week • Resume warfarin therapy at a reduced dose once INR approaches therapeutic range • If bleeding risk is high¶ consider Prothrombinex-VF, 15–30IU/kg • Measure INR in 12–24h. Close monitoring over the following week • Resume warfarin therapy at a reduced dose once INR approaches therapeutic range

INR=international normalised ratio. IV =intravenously

¶ Recent major bleed (within previous 4 weeks) or major surgery (within previous 2 weeks), thrombocytopenia (platelet count, <50□109/L), known liver disease or concurrent antiplatelet therapy

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