

How to reverse warfarin

Index: [Anticoagulation](#)

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Resources



[Warfarin reversal: consensus guidelines, on behalf of the Australasian Society of Thrombosis and Haemostasis \[Position Statement\]](#)

Warfarin is an increasingly commonly used medication in Australia. It is invaluable as an oral anticoagulant and until the oral direct antithrombin agents (e.g., [ximelagatran](#)) (1) are released, it is the only oral medication that can provide “therapeutic” levels of anticoagulation.

Unfortunately, with its increased use, over-anticoagulation has become a common presentation to the emergency department. A high [INR](#) with or without bleeding complication is not an uncommon scenario for hospital inpatients as well (IMHO due in part due to poor warfarin initiation and management).

Guideline for raised INR (adapted from the consensus guidelines) (2):

Clinical setting	Action
INR higher than the therapeutic range but < 5.0; bleeding absent	<p>Lower the dose or omit the next dose of warfarin. Resume therapy at a lower dose when the INR approaches therapeutic range.</p> <p>If the INR is only minimally above therapeutic range (up to 10%), dose reduction may not be necessary.</p>
INR 5.0–9.0; bleeding absent	<p>Cease warfarin therapy; consider reasons for elevated INR and patient-specific factors.</p> <p>If bleeding risk is high, give vitamin K (1.0–2.0 mg orally or 0.5–1.0 mg intravenously).</p> <p>Measure INR within 24 hours, resume warfarin at a reduced dose once INR is in therapeutic range.</p>
INR > 9.0; bleeding absent	<p>Where there is a low risk of bleeding, cease warfarin therapy, give 2.5–5.0 mg vitamin K orally or 1.0 mg intravenously. Measure INR in 6–12 hours, resume warfarin therapy at a reduced dose once INR < 5.0.</p> <p>Where there is high risk of bleeding, cease warfarin therapy, give 1.0 mg vitamin K1</p>

	intravenously. Consider Prothrombinex-HT (25–50 IU/kg) and fresh frozen plasma (150–300 mL), measure INR in 6–12 hours, resume warfarin therapy at a reduced dose once INR < 5.0.
Any clinically significant bleeding where warfarin-induced coagulopathy is considered a contributing factor	<p>Cease warfarin therapy, give 5.0–10.0 mg vitamin K intravenously, as well as Prothrombinex-HT (25–50 IU/kg) and fresh frozen plasma (150–300 mL), assess patient continuously until INR < 5.0, and bleeding stops.</p> <p style="text-align: center;"><i>or</i></p> <p>If fresh frozen plasma is unavailable, cease warfarin therapy, give 5.0–10.0 mg vitamin K intravenously, and Prothrombinex-HT (25–50 IU/kg), assess patient continuously until INR < 5.0, and bleeding stops.</p> <p style="text-align: center;"><i>or</i></p> <p>If Prothrombinex-HT is unavailable, cease warfarin therapy, give 5.0–10.0 mg vitamin K intravenously, and 10–15 mL/kg of fresh frozen plasma, assess patient continuously until INR < 5.0, and bleeding stops.</p>

Prevention: reduce the risk of high INR

The best way to avoid warfarin reversal is to try to prevent the scenarios that lead to a high INR. The following should be considered:

- As per my article on [“how to start warfarin therapy”](#) avoid loading doses of warfarin and initiation schemes designed to reach an INR of 2.0 as quickly as possible for discharge; it is a sure fire recipe for a high INR one to two weeks post discharge in the community (3).
- Patience is importance – unless there is a very good reason, INR need only be tested no more than once a week and each dosage change should be small and well considered.
- Continuing patient education is important.
- Ensure medication compliance before increasing the dose.
- Aim for an INR of 2.5 (the therapeutic range for most conditions is between 2.0 and 3.0 and for mechanical heart valves 2.5 to 3.5 – either way, aiming for 2.5 covers both bases).

There has recently been some discussion about low-intensity warfarin therapy with a target INR of 1.5 to 2.0. However, the “Extended Low-Intensity Anticoagulation for Thrombo-Embolism Investigators” found in 2003 that low-intensity warfarinisation was not as good as standard warfarinisation and did not reduce the rate of bleeding complications (4). As such this practice cannot be recommended.

What to do for INR < 3.5

The increased risk of bleeding is around twice that of an INR from 2.0-3.0. Keep this in

perspective. If there is a 1% per annum risk of serious bleed, an INR of 3.5 means approximately 2% per annum risk; or a miniscule risk that they will have a serious bleed within the next week.

What you will do somewhat depends on the scenario.

- If someone's INR is known to fluctuate up and down but has otherwise been fairly stable on a particular dose, then it would not be unreasonable to keep them on the current dose and repeat the INR in a week.
- Similarly, if there is a good reason for the increase (e.g., commencement of a short course of oral antibiotics), then there is no particular reason to change the existing dose.
- If it appears that the raised INR is likely to remain raised on their current maintenance dose of warfarin, then it would be reasonable to reduce the regular dose to what is estimated to be the correct dose (example, approximately a 10-20% dose reduction) and then recheck the INR in 1-2 weeks.
- Avoid the (IMHO, bad) practice of withholding doses at this INR range.

What to do for INR 3.5 – 5.0

The risk of bleeding is up to quadrupled from an INR of 2.0-3.0. Again keep this in perspective. The absolute risk of a serious bleed in the next few days to week when you will be managing it is very low if the patient doesn't have risk factors.

- Consider precipitating factors, e.g., drug interactions, medication compliance issues. If the INR of 5.0 was unexpected, then it may be reasonable to repeat the INR daily for the next few days to monitor the trend.
- If the patient is otherwise relatively stable, reduce the dose to what would be expected to be the "correct" dose (approximately 20% dose reduction) and check again in a week.
- For some patients who may have higher risk, it is reasonable to repeat the INR on a daily basis and withholding warfarin until the INR falls to below 3.5. At that time, restart at what is estimated as the appropriate dose.

What to do for INR 5.0 – 9.0

The risk of acute bleeding is now raised significantly enough that warfarin should be ceased immediately. The cause of the raised INR should be carefully considered.

- I would advise daily INRs and restarting warfarin once the INR is below 3.5. The dose chosen should be the estimated maintenance dose.
- Try to avoid the inevitable INR "undershoot" by restarting warfarin sooner rather than later once the INR trend is clearly downwards.
- If bleeding risk is high, give a low dose of [vitamin K](#):
 - 1-2 mg orally or;
 - 0.5-1.0 mg intravenously.
- Avoid high doses of vitamin K as it results in "resistance" during re-warfarinisation. Even a small dose intravenously often leads to completely reversal.
- If INR is sub-therapeutic after reversal, then remember to provide alternate forms of anticoagulation (e.g., with [low molecular weight heparin](#)) if indicated.

What to do for INR > 9.0

There is marked increased risk for acute bleeding at this level.

- Again, consider why the INR is raised.
- Immediately cease warfarin therapy.
- Where bleeding risk is low, give vitamin K:
 - 2.5-5.0 mg orally or;
 - 1 mg intravenously.
- Where bleeding risk is high:
 - vitamin K 1 mg intravenously or;
 - Prothrombinex 25-50 units/kg intravenously or;
 - fresh frozen plasma (FFP) 150-300 mL (1 unit) intravenously.
- Check the INR in 6 hours and monitor with daily INRs for the next few days.
- Restart warfarin at the estimated appropriate dose for maintenance when the INR < 5.0.

How to give intravenous vitamin K

In the hospitals I worked in, phytomenadione (vitamin K) (Konakion) tablets were simply not stocked. However, intravenous vitamin K is almost universally available.

Be aware that intravenous vitamin K (also Konakion) comes in both paediatric (2 mg/0.2 mL) and adult (10 mg/1 mL) sizes.

Firstly, insert an intravenous cannula, preferable 21 gauge or larger. Make sure that the line is patent by giving it a flush with sterile saline.

Secondly, ensure that resuscitation equipment is available as intravenous vitamin K can provoke anaphylactic reactions.

Now, the usual dose for intravenous vitamin K is 1 mg, or 0.1 mL. That is impossible to infuse slowly. So:

Draw 10 mg (1 mL) of vitamin K into a 10 mL syringe

Then draw up sterile 0.9% NaCl solution into the syringe to make up 10 mL

Slowly infuse 1 mg (1 mL) of the diluted solution through the cannula over 30-60 seconds

Afterwards, flush with 5-10 mL of saline – again, slowly over 30-60 seconds. For larger doses of vitamin K, infuse the appropriate amount. When diluted up to 10 mL, the concentration of vitamin K is 1 mg/mL.

The INR should always be checked after 6 hours to ensure adequate reversal of anticoagulation.

Reference articles

(1) Brighton TA. The direct thrombin inhibitor melagatran/ximelagatran. *MJA* 2004; 181: 432–437 [download [PDF](#) :: 344 Kb]

(2) Baker RI., Coughlin PB., Gallus AS., et al.; the Warfarin Reversal Consensus Group. Warfarin reversal: consensus guidelines, on behalf of the Australasian Society of Thrombosis and Haemostasis [Position Statement]. *MJA* 2004; 181 (9): 492-497 [download [PDF](#) :: 183 Kb]

(3) Tam M. How to start warfarin therapy [electronic article]. *The Medicine Box*. Last updated 20 July 2006. [[Link](#)]

(4) Kearon C., Ginsberg JS., Kovacs MJ., et al.; Extended Low-Intensity Anticoagulation for Thrombo-Embolic Investigators. Comparison of low-intensity warfarin therapy with conventional-intensity warfarin therapy for long-term prevention of recurrent venous thromboembolism. *New England Journal of Medicine*. 349(7):631-9, 2003 Aug 14 [download [PDF](#) :: 910 Kb]

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