BERIPLEX® NZ dosing guidance

Key points applicable to all tables:

In patients > 100 kg, the dose of BERIPLEX® NZ should be calculated based on a capped 100 kg body weight and maximum dose of 50 IU/kg **(i.e., the maximum absolute dose is 5000 IU).**

Repeat dosing is not supported by clinical data and the product information documents the risk of thrombosis with repeat dosing . If repeat dosing is required within 14 days* discuss this requirement with a NZBS Transfusion Medicine Specialist (TMS).

*The interval for repeat dosage requiring consultation has been estimated based on >95% elimination of Factor II, which at 60 hours has the longest serum half-life of all the active ingredients.

Elevated INR

Increased INR is associated with increased bleeding risk depending on the patient's condition and comorbidities. Consensus recommendations identify risk factors to consider and measures to reduce the risk.

Table 4. Management considerations for increased INR

Patient Risk Factors[5]	Risk-reduction of supratherapeutic INR (> 4.5)[6]
• Age • Prior bleeding history • Concomitant medications (especially aspirin and non-steroidal anti-inflammatory drugs) • Medical comorbid conditions (e.g. deranged renal and liver function)	• Regular INR monitoring, especially during episodes of illness or hospitalisation • Avoidance of concomitant medications that can result in INR lability

Source: Updated recommendations for warfarin reversal in the setting of four-factor prothrombin complex concentrate (2024) on behalf of the Thrombosis & Haemostasis society of Australia and New Zealand (THANZ).

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Abbreviations

3FPCC = three-factor prothrombin complex concentrate

4FPCC = four-factor prothrombin complex concentrate

FPP = Fresh frozen plasma

INR = international normalised ratio

IV = intravenous

NZBS = New Zealand Blood Service

TMS = Transfusion Medicine Specialist

VKA = Vitamin K antagonist

Warfarin Reversal Guidelines

Transfusion Medicine Handbook

Beriplex®-NZ Datasheet

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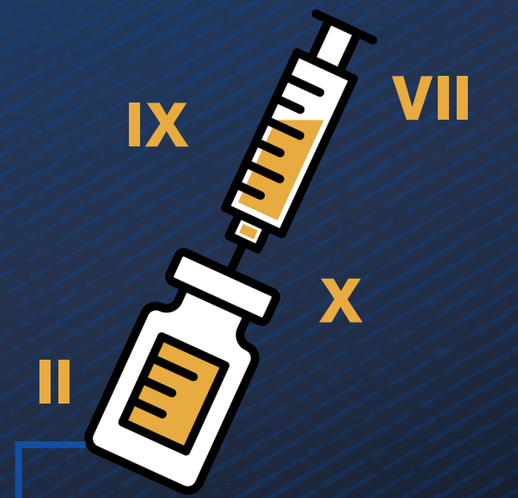
NZBLOOD
Te Ratonga Toto O Aotearoa

Warfarin Reversal
using BERIPLEX® NZ



Information for Healthcare Professionals

Introduction

Warfarin, a vitamin K antagonist (VKA), is a commonly used anticoagulant for patients at risk of arterial or venous thromboembolism. It is effective in the prevention and treatment of a wide range of thrombotic disorders. However, warfarin-associated major bleeding arises in 1-3% of patients annually.[1]

Patients on warfarin with bleeding or who require urgent surgery should receive prompt management. Clinical decisions must balance the risk of bleeding versus the risk of thromboembolism.

A range of therapeutic options exist to reverse the anticoagulant effect of warfarin, including dose modification, vitamin K administration and urgent reversal using a prothrombin complex concentrate (PCC).

In response to the introduction of a four-factor PCC, the Thrombosis & Haemostasis society of Australia and New Zealand (THANZ) revised their recommendations for the urgent reversal of warfarin in 2024[2], aligning practice to international guidelines.

Change to urgent warfarin reversal management with 4FPCC

In New Zealand, the 4FPCC available is BERIPLEX® NZ, containing factors II, VII, IX and X. For urgent warfarin reversal, THANZ guidelines[2] advise:

- The addition of factor VII in BERIPLEX® NZ removes the need for co-administration of fresh frozen plasma (FFP)
- Vitamin K administration is still indicated to achieve a more sustained reversal

In emergency warfarin reversal, 4-factor PCCs have greater than three times the odds of achieving the goal international normalized ratio (INR)[3] than 3-factor PCCs.

Significant increases in vitamin K dependent factors occur within five minutes of infusion.[4]

Comparison of 3FPCC and 4FPCC

Table 1. Comparison of warfarin reversal with 3FPCC (PROTHROMBINEX® VF) versus 4FPCC (BERIPLEX® NZ)

	Previously published guidelines: 3FPCC (Prothrombinex-VF)	New guidelines: 4FPCC (Beriplex)
Management of patients on warfarin therapy with bleeding	• Co-administration of FFP in addition to Prothrombinex-VF • INR ≥ 2 with clinically significant bleeding: 35-50 IU/kg IV Prothrombinex-VF	• No requirement for additional administration of FFP • INR ≥ 2 with clinically significant bleeding: 25-50 IU/kg IV Beriplex #
Management of non-bleeding patients on warfarin (e.g. before urgent surgery)	Unchanged	Unchanged

In patients > 100 kg, the dose of BERIPLEX® NZ is calculated based on a capped 100 kg body weight and **maximum dose of 50 IU/kg** (i.e., the maximum absolute dose is 5000 IU).

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4FPCC to reverse warfarin: bleeding present

Table 2. Management of patients on warfarin therapy with bleeding

Clinical setting	Recommendations
INR ≥ 1.5 with life threatening or critical organ bleeding	Omit warfarin therapy and administer: • Vitamin K 5.0-10.0 mg IV; and • 4FPCC 50 IU/kg*#
INR ≥ 2.0 with clinically significant bleeding (not life-threatening)	Omit warfarin therapy and administer: • Vitamin K 5.0-10.0 mg IV; and • 4FPCC 25-50 IU/kg # based on INR and patient level factors (e.g. type of bleeding, need and ability to undergo intervention)
Any INR with minor bleeding	• Omit warfarin • Repeat INR and adjust warfarin dose to maintain INR in the target therapeutic range • If bleeding risk is high or INR > 4.5, consider vitamin K (1.0-2.0 mg orally, or 0.5-1.0 mg IV)

*Consider administering a 4FPCC dose < 50.0 IU/kg when INR 1.5-1.9.

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4FPCC to reverse warfarin: before surgery

Table 3. Suggested 4FPCC# dosing for warfarin reversal in non-bleeding patients (e.g. before surgery^)

	Initial international normalised ratio (INR)			
Target INR	**1.5-2.5**	**2.6-3.5**	**3.6-10.0**	**> 10.0**
0.9-1.3	30 IU/kg	35 IU/kg	50 IU/kg	50 IU/kg
1.4-2.0	15 IU/kg	25 IU/kg	30 IU/kg	40 IU/kg

^Outside of the peri-operative setting, 4FPCC use should only be considered if INR >10 and there is a high risk of bleeding.

In patients > 100 kg, the dose of BERIPLEX® NZ is calculated based on a capped 100 kg body weight and **maximum dose of 50 IU/kg** (i.e., the maximum absolute dose is 5000 IU).

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For patients on long-term warfarin who urgently or emergently require reversal of warfarin therapy before an invasive procedure, please dose BERIPLEX® NZ according to Table 3. If BERIPLEX® NZ is not available, transfuse 10-15 mL/kg of plasma.

For elective and non-urgent procedures, please consult with haematology and/or anaesthesia as per local policy about the appropriateness of continuing warfarin therapy or using bridging anticoagulation during the periprocedural period.