# ORAL ANTICOAGULANTS IN TRAUMA GUIDELINE



## 1. Key Messages

The Victorian State Trauma System provides support and retrieval services for critically injured patients requiring definitive care, transfer and management. This guideline provides evidence based advice on the management of patients who present to Victorian health services who are involved in trauma while taking oral anticoagulant medication.

This guideline is developed for all clinical staff involved in the care of trauma patients in Victoria. It is intended for use by frontline clinical staff who provide early care for major trauma patients; those working directly at the Major Trauma Service (MTS) as well as those working outside of a MTS. These management guidelines provide up-to-date information for frontline healthcare clinicians.

These guidelines provide the user with accessible resources to effectively and confidently provide early care for critically injured bleeding patients on oral anticoagulants. The guideline has been assessed utilising the AGREE II methodology for guideline development and is under the auspice of the Victoria State Trauma Committee (VSTC).[1]

### Clinical Emphasis Points:

- Early identification of the trauma patients' coagulation status is vital to their initial management.
- It is important for all emergency care providers to be familiar with the mechanism of action of oral anticoagulants and to understand how standard coagulation testing is affected.
- In small rural health services/urgent care services not all management guidelines are able to be undertaken particularly coagulation testing. Health services are expected to provide care as close as possible to management principles.

- Some of the new oral anticoagulants do not have direct antidotes therefore management should focus on resuscitation and factor replacement
- Knowledge of agents that reverse anticoagulation is essential for managing acute, traumatic haemorrhage.
- For bleeding patients on oral anticoagulants, early consultation with the MTS emergency, trauma and haematology staff via ARV is advised to assist in directing patient care and to facilitate early retrieval.
- Any patient who is taking an anticoagulant is at high risk of developing a significant intracranial haemorrhage from minor head injury mechanisms.

Victorian State Trauma System Guideline

# Anticoagulation in Trauma

RAUMA VICTORIA

## Make early contact with ARV for advice from the major trauma services and to initiate retrieval.

- Early identification of coagulation status is vital to initial management.
- Bleeding can rapidly become life threatening in the patient taking oral anti-coagulants.
- Early consultation with trauma services and haematologist via ARV will guide ongoing management.

### Initial Assessment

- Complete primary survey and identify likely source and level of bleeding.
- Identify which Oral Anti-Coagulant (OAC) the patient is taking and time of last dose.
- Perform baseline laboratory assessment: Hb, APTT, INR if on Warfarin and where available specific drug levels.
- Creatinine should be measured to identify presence of any pre-existing renal or hepatic impairment.
- Organise blood group and hold, antibody screen.

**Early consultation with trauma services and haematologist via ARV is advised to direct treatment and to facilitate early retrieval**

| | | | |
|---|---|---|---|
| **Mild Bleeding** | • Local haemostatic measures.<br>• Consider withholding next dose of OAC or discontinue as appropriate (thrombosis vs bleeding risk). | | |
| **Clinically significant bleeding**<br>(reduction in Hb >20g/L, transfusion of >2 units of red cells in 1 hr) | • Administer oral charcoal if OAC ingested <2 hr prior (if safe to do so) and discontinue OAC.<br>• Apply local haemorrhage control techniques & consider surgical or radiological intervention to identify and treat bleeding source<br>• Maintain adequate hydration to aid in drug clearance.<br>• Transfusion of red cells should be administered as clinically appropriate. Platelet transfusion should be considered in patients on concurrent anti platelet therapy or with significant thrombocytopenia (platelet <50 x 109/L). Use FFP if concerned about dilutional coagulopathy.<br>• Contact retrieval services for haematology advice and to initiate retrieval & transfer to a MTS.<br>• Continuously monitor haemodynamic status. | | |
| **Life threatening bleeding**<br>(bleeding in critical area or organ (intraocular, intracranial, intraspinal, compartment syndrome, retroperitoneal or pericardial), hypotension not responding to resuscitation). | **Vitamin K Antagonist**<br>(Warfarin) | **Direct Factor Xa inhibitor**<br>(Rivaroxaban, Apixaban) | **Direct Thrombin inhibitor**<br>(Dabigatran) |
| | • Institute above clinical measures.<br>• Consider use of one of the following agents:<br>- *Prothrombinex – VF 25-50 units/kg IV<br>- *FEIBA 50 IU/kg.<br>- Tranexamic acid 15-30 mg/kg IV +/- infusion for mucosal bleeds.<br>- Vitamin K 5-10mg slow IV injection for full reversal in 12-24 hours (only if on Warfarin). | • Institute above clinical measures.<br>• Consider use of one of the following agents:<br>- *Prothrombinex – VF 25-50 units/kg IV<br>- *FEIBA 50 IU/kg.<br>- Tranexamic acid 15-30 mg/kg IV +/- infusion for mucosal bleeds.<br>- Recombinant factor VIIa (Novoseven) IV bolus 50mcg/kg may be trialled if critical bleeding. Discuss with haematology. Patient approval should be obtained as per local procedure for its use in non-haemophiliac patients who have failed to respond to conventional therapy. | • Institute above clinical measures.<br>• Consider use of one of the following agents:<br>- *Prothrombinex – VF 25-50 units/kg IV.<br>- *FEIBA 50 IU/kg.<br>- Tranexamic acid 15-30 mg/kg IV +/- infusion for mucosal bleeds.<br>- Vitamin K 5-10mg slow IV injection for full reversal in 12-24 hours (only if on Warfarin).<br>- Consider dialysis for Dabigatran where an excessively prolonged APTT >80s or dabigatran level >500ng/mL and/or impaired renal function. Dialysis can remove approximately 60% of the drug over 3-4 hours.<br>- Consider Idarucizumab administration after haematology approval. The complete dose of 5g should be given as two consecutive IV infusions over 5-10 minutes each no more than 15 minutes apart). |

*This is an off license use of FEIBA and Prothrombinex-VF and the risk of thrombotic complications with these agents when used for this indication is unclear. Their use is supported by laboratory data but clinical evidence supporting the improvement in patient outcomes is lacking.

*Adapted from Tran, H. Joseph, J. Young, L. McRae, S. Curnow, J, Nandurkar, H. Wood, P. and McLintock, C. New oral anticoagulants: a practical guide on prescription laboratory testing and peri-procedural / bleeding management. Int Med J. 2014;(44):525-36*

# 3. Introduction

The use of long-term oral anticoagulant (OAC) therapy for the treatment and prevention of thrombosis and thromboembolism is widespread. Emergency providers are likely to encounter patients on OACs on a regular basis. Warfarin remains the most commonly prescribed oral anticoagulant in Australia, prescribed for the management of chronic atrial fibrillation (AF) in order to prevent stroke, to prevent thrombus formation in patients with mechanical heart valves (MHV's) and for treatment of venous thromboembolisation (VTE).[2]

Vitamin K antagonists (Warfarin) are one of the oldest anticoagulants on the market having been in clinical use for over 60 years. With the development of newer medications, there is a now a range of anticoagulant therapy options available including Direct Xa inhibitors (Rivaroxiban and Apixaban) and direct Thrombin inhibitors (Dabigatran). Each have advantages and disadvantages as well as elimination times and reversal requirements.

The assessment and management of the trauma patient who is anticoagulated pre-injury adds additional complexity to an already difficult presentation. Bleeding has been found to be one of the main causal factors of mortality after physical injury (30-40%) and should be regarded as potentially reversible.[3] Other factors which may contribute to the risk of bleeding include age >65 years, steroid use, malnutrition, hepatic insufficiency, renal failure, underlying malignancy, excessive alcohol use, platelet dysfunction as well as the use of therapies that affect platelet function such as aspirin, clopidogrel and NSAIDs.[4]

Clinicians must act quickly to ascertain the level of bleeding and to identify patient's regular medications, coagulation status and the most appropriate method of reversal if indicated. If the patient is under the effects of anticoagulant medications, the risk of bleeding is increased, especially if it cannot be reversed quickly. Further complication to the patients care is from the concurrent medical comorbidities for which the patient is anticoagulated. Questioning the patient or family members regarding the patient's coagulation status should become a part of routine questioning, particularly among older patients.

While most patients presenting to the ED who are taking OACs are likely to be taking Warfarin, it is important for all emergency care providers to gain familiarity with the newer or direct OACs (DOACs), previously termed novel oral anticoagulants (NOAC) and to understand how standard coagulation testing is affected.

# 4. Types of oral anticoagulation

## Vitamin K Antagonists

### *Warfarin*

Warfarin is a type of vitamin K antagonist which acts by working against vitamin K in the liver. Common indications for its use is in stroke prevention in atrial fibrillation (AF), preventing thrombus formation in patients with mechanical heart valves (MHV), and treatment of venous thromboembolism (VTE). Warfarin has been prescribed for over 50 years, it is well understood and there is a large history of experience in its clinical use. The effect of treatment is easy to measure and to monitor compliance with treatment. The widespread use of Warfarin will likely continue among patients who are already stable, have

severe renal impairment and for anticoagulant indications for which the newer novel agents have not been evaluated, such as MHV.[2] Reversal can be achieved with Vitamin K and Prothrombin Complex Concentrate (PCC).

## Direct (or Novel) Oral Anticoagulants (DOAC's/NOAC's)

*Direct Xa Inhibitor (Rivaroxaban, Apixaban)*

*Direct Thrombin Inhibitors (Dabigatran)*

The novel or new oral anticoagulants (NOACs) are a group of drugs recently introduced to Australia (2013) that act as either a direct thrombin inhibitor or a direct inhibitor of Factor Xa. These agents have been shown to provide excellent clinical reduction in thrombosis with an acceptable bleeding profile. All have a simple fixed dosing whether daily or twice daily, and no significant dietary interactions. DOAC's are at least equivalent to warfarin with respect to prevention of stroke and systemic embolization with some showing statistical superiority. Lower rates of major bleeding were found, with a significant reduction in the rate of intracranial haemorrhage.[5] A wide therapeutic window enables fixed dosing in adults without the need for laboratory monitoring.

*Clopidogrel*

- Clopidogrel is an anti-platelet drug that that inhibits the ability of platelets to clump together as part of a blood clot. Clopidogrel prevents blood clots by irreversibly binding to the P2Y12 receptor on platelets, preventing adenosine diphosphate (ADP) from activating platelets. It belongs to a class of drugs called P2Y12 inhibitors.[6]

*Ticagrelor*

- Ticagrelor is an oral antiplatelet drug, it inhibits platelet aggregation by blocking the platelet P2Y adenosine disphosphate receptor, ticagrelor binds reversibly, so its inhibitory effect on platelet aggregation is more quickly reversed. Ticagrelor is given in combination with aspirin for the treatment of acute coronary syndrome. There is no current reversal agent.[7]

## Half-life and Elimination[8]

| DRUG | HALF LIFE | ELIMINATION |
|---|---|---|
| Warfarin | 35 hours | Hepatically metabolised, renal and faecal excretion |
| Rivaroxaban | 5-9 hours (healthy)<br>11-13 hours (elderly) | 67% renal (half is inactive drug), 33% faecal |
| Apixaban | 8-15 hours | 25% renal, 75% faecal |

| | | |
|---|---|---|
| Dabigatran | 12-17 hours (prolonged in renal impairment) | 80% renal. Diuresis must be maintained to promote adequate drug clearance. |
| Clopidogrel | 6 hours | 50% urine, 50% faeces |
| Ticagrelor | 9 hours | Metabolism by CYP-450 enzymes |

# 5. Monitoring / Pathology tests

Standard laboratory INR/APTT tests are difficult to interpret in the presence of the newer oral anti-coagulation medication. Early haematologist consultation is advised to assist interpretation of the results and assess risk of bleeding.

### *International Normalised Ratio (INR)*

The International Normalised Ratio (INR) is the PT ratio corrected for the sensitivity of the thromboplastin used in the test. INR is a standardised measurement of how long it takes blood to form a clot. The coagulation factors II, VII, IX and X are dependent on Vitamin K for synthesis & are reflected by the INR. It is used to determine the effects of oral Warfarin on the clotting system and to monitor levels so that a therapeutic range for dosing can be adjusted accordingly. For most warfarin indications, the target INR is 2.0-3.0 (VTE and single MHV excluding mitral). For mechanical mitral valve or combined mitral and aortic, the target INR is 2.5 -3.5.

The modes of action of DOAC's differ from that of warfarin and their effect cannot be determined by INR testing.

### *Prothrombin Time (PT)*

Evaluates coagulation factors VII, X, V, II and I (fibrinogen). Measures the speed of clotting by means of the extrinsic pathway (also known as the tissue factor pathway). Warfarin typically prolongs the PT alone, but at high levels can prolong aPTT also. For rivaroxaban & apixaban, the PT may be prolonged with the presence of a significant dose of the drug.

### *Activated Partial Thromboplastin Time (aPTT)*

Evaluates coagulation factors XII, XI, IX, X, V, II (prothrombin) and I (fibrinogen). Measures the overall speed at which blood clots by means of reactions known as the intrinsic and common coagulation pathways. The typical reference range is between 30 – 40 seconds.

aPTT is moderately sensitive to Dabigatran. At peak therapeutic plasma concentrations, the aPTT is increased up to 2 times and at trough concentrations (e.g., 12 hours after the last dose) it falls to approximately 1.3 times control values.[9] Trough APTT values greater than 80 seconds are associated with increased bleeding risk.[10] The time between the last dose of dabigatran and blood collection must be determined as it will affect the results. The aPTT may also be mildly prolonged in the presence of apixaban and rivaroxaban.

### *Fibrinogen assay*

Fibrinogen is a protein that is essential for blood clot formation and a reflection of clotting ability and activity in the body. Reduced concentrations of fibrinogen may impair the body's ability to form a stable blood clot and are seen at an early stage in severe haemorrhage.

### *Viscoelastic tests*

Thromboelastography (Rotem or TEG) are point of care analysers that provides rapid information on global haemostasis and is used to guide transfusions in perioperative and trauma settings.

It provides information on the whole kinetics of haemostasis: clotting time, clot formation, clot stability and lysis.[11] By combining and comparing the results from different ROTEM tests, it is possible to identify single or multiple coagulation factor deficiencies within a few minutes of obtaining samples and goal-directed coagulation therapy can be readily initiated.[12]

## Interpretation of coagulation screen

### *Warfarin*

- Prolongs the PT more than APTT
- PT/INR is used to monitor anticoagulation

### *Apixaban/Rivaroxaban/Dabigatran*

Early haematologist consultation is advised regarding the effect of these medications and interpretation of coagulation testing as there are no clear correlates.

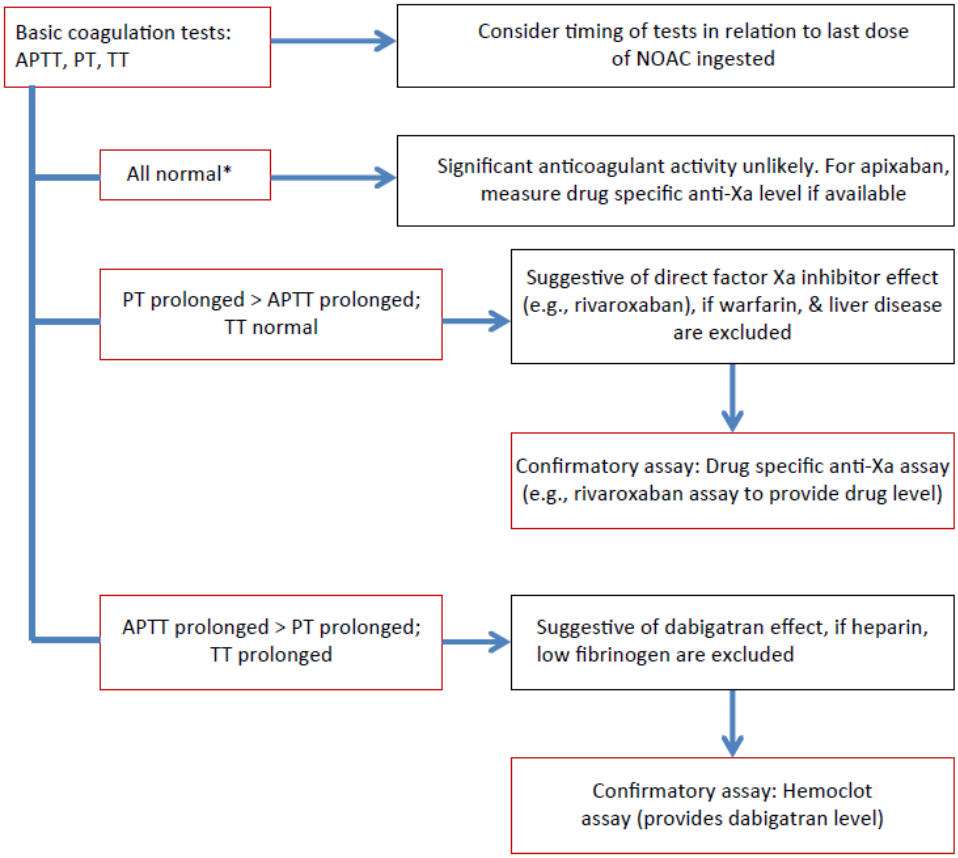


Figure 1: Suggested laboratory algorithm for dabigatran and rivaroxaban evaluation

*Routine coagulation tests are insensitive to apixaban.

Taken from Tran, H. Joseph, J. Young, L. McRae, S. Curnow, J, Nandurkar, H. Wood, P. and McLintock, C. New oral anticoagulants: a practical guide on prescription laboratory testing and peri-procedural / bleeding management. Int Med J. 2014;(44):525-36

## 6. Management agents

While the effects of Warfarin can be reversed, some of the newer oral anticoagulants do not have direct antidotes therefore management should focus on resuscitation and factor replacement.[13]

Early haematological advice from the MTS's is recommended to guide management.

### *Vitamin K*

Vitamin K, given orally or intravenously (Phytomenadione) can be used to accelerate Warfarin reversal by counteracting its effects on Vitamin K-dependent coagulation factor synthesis.[9] The intravenous route achieves a more rapid response compared with oral administration, with an onset of action seen within 6-8 hours.[2] Its effect is not immediate

but will progress over time as the liver synthesises sufficient quantities of coagulation proteins (factors II, VII, IX, X) dependant on Vitamin K.

The usual does is 5-10mg IV given as a bolus dose.

## Transfusion support

### *Fresh Frozen Plasma (FFP)*

Replacement is required to correct the low levels of factors II, VII, IX and X induced by warfarin. FFP contains all coagulation factors present in whole blood but it is not a factor concentrate therefore multiple units may be required.

The use of plasma requires the treating facility to have appropriate facilities for frozen plasma storage and thawing. The patients' blood group must be determined (or group AB plasma may be used) and the time taken for infusion are all be factors to be considered.[2]

## Anti-fibrinolytic agents

### *Tranexamic Acid (TXA)*

Consideration of the use of the anti-fibrinolytic agent TXA IV 15-30mg/kg, followed by a continuous infusion at 1mg/kg/hr until bleeding is under control in Factor Xa inhibitors. There is limited evidence of the clinical benefit for TXA in this setting and treatment should not delay resuscitative efforts.[14]

## Pro-haemostatic agents

### *Prothrombin Complex Concentrates (PCC's)*

Prothrombinex-VF is the only PCC product currently available for use in Australia and NZ for warfarin reversal. It is a three factor PCC (II, IX and X) with low levels of factor VII. Prothrombinex-VF can be rapidly reconstituted into a small volume for infusion over a few minutes with a fast onset of action. The early use of PCC is recommended for the emergency reversal of Vitamin K dependant oral anticoagulants (Warfarin).

Prothrombinex-VF is able to completely reverse an elevated INR within 15 minutes but due to the short half-life should be supplemented with Vitamin K to sustain the effect.[2] In patients with life threatening bleeding, supplementing factor VII by administration of FFP should ensure optimal reversal of the anticoagulant effect of warfarin.

Reversal of Direct Factor Xa inhibitors (Rivaroxaban, Apixaban) cannot be achieved with PCC however, small doses of PCC will optimise coagulation in the presence of vitamin K deficiency or unknown co-administration of vitamin K antagonists and may act as a partial bypassing agent in very high doses and can be considered in extreme cases. PCC is not suggested for use in patients being treated with direct thrombin inhibitors (Dabigatran).[15] A specific reversal agent, Idarucizumab, is available in some centres for reversal of Dabigatran (see below).

The use of PCC does carry the increased risk of venous and arterial thrombosis during the recovery period, therefore careful consideration of its use should be weighed against the need for rapid correction of coagulopathy.

*Recombinant Factor VIIa – rFVIIa (Novoseven)*

rFVIIa is a novel agent used to control intractable haemorrhage. rFVIIa promotes the formation of clots by activating the extrinsic clotting cascade which leads to thrombin converting fibrinogen to fibrin.

Ideally, the following should be present before rFVIIa administration:

- Haematocrit >24%
- pH>7.2
- platelets >50 x 10E9/L
- fibrinogen >1.0g/L

An IV Bolus of 50mcg/kg may be trialled if critical bleeding from Factor Xa inhibitors. Each hospital setting will have its own local procedure for the use of Novoseven in the management of life threatening bleeding.

### Reversal agents

*Idarucizumab*

Idarucizumab is a monoclonal antibody fragment which binds free and thrombin-bound dabigatran and neutralises its activity, resulting in complete reversal of the anticoagulant effect. Its effect is immediate and lasts for 24 hour.[16]

The complete dose of 5g should be given as two consecutive IV infusions over 5-10 minutes each. As it is a fairly new drug on the scene, its availability is limited and in Victoria is only located at The Alfred and Royal Melbourne Major Trauma Centres.

## 7. Early management

**FOR BLEEDING PATIENTS ON ORAL ANTICOAGULANTS, EARLY CONSULT WITH THE MTS EMERGENCY, TRAUMA AND HAEMATOLOGY STAFF VIA ARV IS ADVISED TO ASSIST IN DIRECTING PATIENT CARE AND TO FACILITATE EARLY RETRIEVAL.**

*Initial assessment*

- Complete primary survey and identify likely source and level of bleeding
- Identify which OAC patient is taking and time of last dose
- Perform baseline laboratory assessment: FBC, routine coagulation studies, INR if on Warfarin and where available specific drug levels. Creatinine should be measured to identify presence of any pre-existing renal or hepatic impairment
- Organise blood group and hold, antibody screen

*Mild Bleeding*

- Local haemostatic measures
- Consider withholding next dose of anticoagulant or discontinue treatment as appropriate (thrombosis vs bleeding risk)

- Consider the risk of worsening bleeding. Early reversal or replacement of factors may prevent worsening of bleeding

*Clinically significant bleeding (reduction in Hb ≥20g/L, transfusion of ≥2 units of red cells)*

- Administer oral charcoal if OAC ingested <2 hr prior and discontinue OAC
- Apply local haemorrhage control techniques & consider surgical or radiological intervention to identify and treat bleeding source
- Maintain adequate hydration to aid in drug clearance
- Transfusion of red cells should be administered as clinically appropriate. Platelet transfusion should be considered in patients on concurrent anti platelet therapy or with significant thrombocytopenia (platelet <50 x $10^9$/L). Use FFP if concerned about dilutional coagulopathy. [17]
- Contact retrieval services for haematology advice and to initiate retrieval & transfer to a MTC
- Continuously monitor haemodynamic status
- In addition:
    - Consider administration of Vitamin K if patient is on Warfarin

*Life threatening bleeding (bleeding in critical area or organ (intraocular, intracranial, intraspinal, compartment syndrome, retroperitoneal or pericardial), hypotension not responding to resuscitation*

- Institute above clinical measures
- Consider use of one of the following agents:
    - *Prothrombinex – VF 25-50 units/kg IV
    - *FEIBA 50 IU/kg
    - Tranexamic acid 15-30 mg/kg IV +/- infusion for mucosal bleeds
    - Vitamin K 5-10mg slow IV injection for full reversal in 12-24 hours (only if on Warfarin)
- Consider dialysis for Dabigatran where an excessively prolonged APTT >80s or dabigatran level >500ng/mL and/or impaired renal function. Dialysis can remove approximately 60% of the drug over 3-4 hours.
- In Dabigatran, consider Idarucizumab administration after haematology approval. The complete dose of 5g should be given as two consecutive IV infusions over 5-10 minutes each no more than 15 minutes apart).
- Recombinant factor VIIa (Novoseven) IV bolus 50mcg/kg may be trialled if critical bleeding from Rivaroxaban and Apixaban. If ongoing bleeding, discuss with haematology. Patient approval should be obtained as per local procedure for its use in non-haemophiliac patients who have failed to respond to conventional therapy.
- Pro-haemostatic agents are unlikely to improve outcome in patients on Rivaroxaban with a normal PT.

**This is an off license use of FEIBA and Prothrombinex-VF and the risk of thrombotic complications with these agents when used for this indication is*

*unclear. Their use is supported by laboratory data but clinical evidence supporting the improvement in patient outcomes is lacking.*

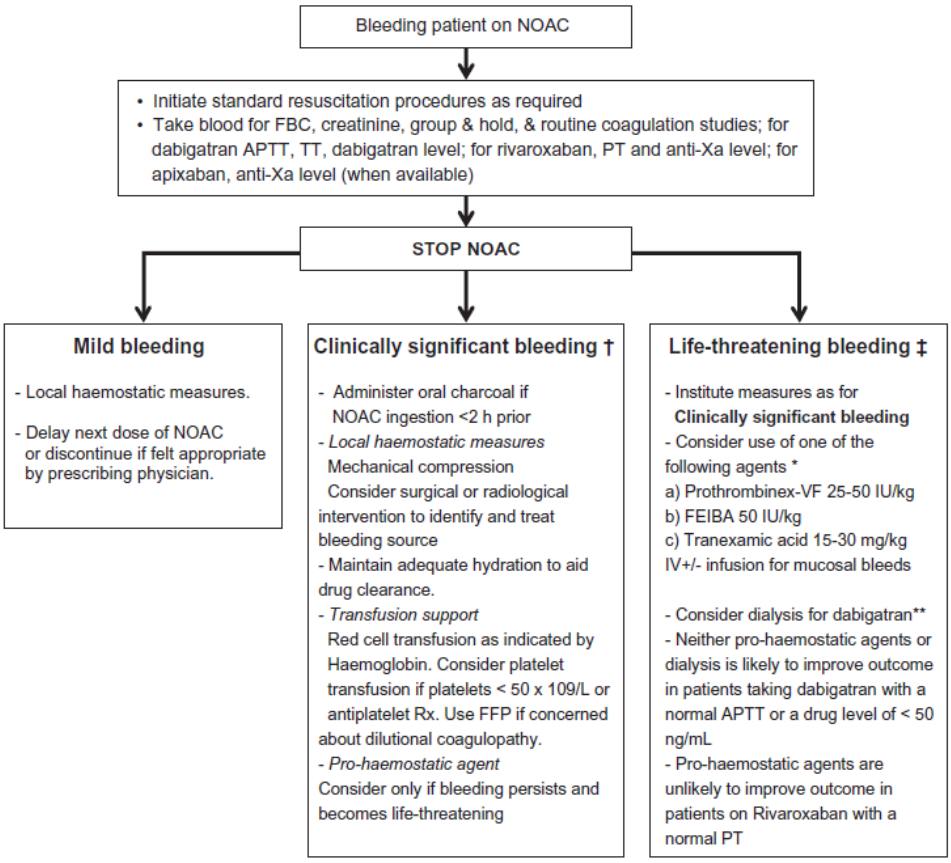


**Figure 3** Management of new oral anticoagulants (NOAC)-associated bleeding.[26-31,33,34] †Clinically significant bleeding – reduction in Hb ≥ 20g/L, transfusion of ≥2 units of red cells. ‡Life-threatening bleeding – bleeding in critical area or organ (intraocular, intracranial, intraspinal, compartment syndrome, retroperitoneal or pericardial), hypotension not responding to resuscitation. *This is an off license use of FEIBA and Prothrombinex-VF and the risk of thrombotic complications with these agents when used for this indication is unclear. Their use is supported by laboratory data but clinical evidence supporting an improvement in clinical outcomes is lacking. **Dialysis is indicated if dabigatran level is high as indicated by excessively prolonged activated partial thromboplastin time (APTT) > 80 s or dabigatran level > 500 ng/mL and/or impaired renal function. Four hours of haemodialysis will reduce drug level by ~60%.[26] FBC, full blood count; FFP, fresh frozen plasma.

Taken from Tran, H. Joseph, J. Young, L. McRae, S. Curnow, J, Nandurkar, H. Wood, P. and McLintock, C. New oral anticoagulants: a practical guide on prescription laboratory testing and peri-procedural / bleeding management. Int Med J. 2014;(44):525-36

## 8. Head Injury and Oral Anticoagulants

*See Traumatic Brain Injury guideline: Early Management*

Any patient who is taking an anticoagulant such as warfarin or other oral anticoagulants (dabigatran, rivaroxaban, apixaban) is at high risk of developing a significant intracranial

haemorrhage from minor head injury mechanisms. CT imaging of the brain should be performed on all patients with a history of head injury.

In addition, platelet inhibitor therapy (aspirin (e.g. Astrix, Cartia), dipyridamole (Asasantin, Persantin), clopidogrel (Iscover, Plavix), prasugrel (Effient), ticagrelor (Brilinta)) also increases the risk for haemorrhagic injuries but to a lesser degree.

These patients often have significant comorbidities also, all of which will have a direct impact on surgical and intensive care decision making and treatment. The effects of anticoagulation and antiplatelet drugs may require their reversal, with consideration of the risks of exacerbation of the underlying condition.

Where intracranial haemorrhage is present, patients on anticoagulation medication may deteriorate because of extension of their bleed leading to mass effect, brain compression and herniation. In these patients, reversal of medications should be commenced with appropriate reversal agents. **Consultation** with ARV should take place prior to administration.

For immediate reversal of anticoagulation in patients with bleeding due to warfarin, prothrombin complex concentrates (Prothrombinex-VF in Australia) are preferred over fresh frozen plasma (FFP). The dose for prothrombin complex concentrates is 35–50 units/kg IV. This aims to achieve complete reversal of an excessive INR within 15 minutes. The dose for life-threatening bleeding should be the maximum 50 units/kg.[2]

In the setting of isolated traumatic brain injury, FFP is not routinely needed in combination with prothrombin complex concentrates unless there is life-threatening bleeding. If life-threatening bleeding is present the dose of FFP is 150–300 mL by IV infusion. Where Prothrombinex-VF is unavailable the dose for FFP is 15 mL/kg IV infusion. Time is required for determining the patient's blood type (or use group AB plasma), thawing of the product and subsequent infusion.

Vitamin K is essential for sustaining the reversal achieved by PCC or FFP. IV administration produces a more rapid response than oral administration in the short term. The dose is 5–10 mg IV.

Anticoagulation should only be restarted after discussion with Neurosurgeons.

## 9. Retrieval and Transfer

For centres that do not carry the majority of reversal medication or have access to a blood bank, the best option is to initiate retrieval and transfer early.

It is important to note that an exhaustive clinical workup and intervention is not always necessary or appropriate prior to transfer. Stabilisation and ensuring life-threatening problems are addressed, as well as taking measures to prevent deterioration en route, are essential aspects of early care. Delaying transfer to obtain laboratory results or imaging studies may delay access to definitive treatment. Often such studies must be repeated at the receiving facility regardless.

In liaison with ARV clinicians, interventions to stabilise the patient prior to retrieval personnel arriving should be commenced. ARV will coordinate the retrieval and will evaluate the practical and clinical needs involved in transferring the patient from the referral hospital. Once retrieval staff arrive on scene, be prepared to give a thorough handover. Retrieval staff

will assess the patient prior to transfer and may make changes to care in order to ensure the patient is safe during transfer.

In consultation with ARV and the MTS, if bleeding is critical and supply is not available at the facility, transport of antidotes / procoagulants can be arranged and brought to site with retrieval staff.

# 10. Appendix 1: AGREEII Score Sheet – Oral anticoagulants in trauma guideline

**AGREE II Score Sheet: Oral anticoagulants in trauma guideline**

| Domain | Item | AGREE II Rating | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | 1 *Strongly Disagree* | 2 | 3 | 4 | 5 | 6 | 7 *Strongly Agree* |
| Scope and purpose | 1. The overall objective(s) of the guideline is (are) specifically described. | | | | | | | X |
| | 2. The health question(s) covered by the guideline is (are) specifically described. | | | | | | | X |
| | 3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described. | | | | | | | X |
| Stakeholder involvement | 4. The guideline development group includes individuals from all the relevant professional groups. | | | | | | X | |
| | 5. The views and preferences of the target population (patients, public, etc.) have been sought. | | | | | | | X |
| | 6. The target users of the guideline are clearly defined. | | | | | | | X |
| Rigor of development | 7. Systematic methods were used to search for evidence. | | | | | X | | |
| | 8. The criteria for selecting the evidence are clearly described. | | | | | | X | |
| | 9. The strengths and limitations of the body of evidence are clearly described. | | | | | | X | |
| | 10. The methods for formulating the recommendations are clearly described. | | | | | | X | |
| | 11. The health benefits, side effects and risks have been considered in formulating the recommendations. | | | | | | X | |
| | 12. There is an explicit link between the recommendations and the supporting evidence. | | | | | | | X |
| | 13. The guideline has been externally reviewed by experts prior to its publication. | | | | | | | X |
| | 14. A procedure for updating the guideline is provided. | | | | | | | X |
| Clarity of presentation | 15. The recommendations are specific and unambiguous. | | | | | | X | |
| | 16. The different options for management of the condition or health issue are clearly presented. | | | | | | | X |
| | 17. Key recommendations are easily identifiable. | | | | | | | X |

| Domain | Item | AGREE II Rating | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | 1 *Strongly Disagree* | 2 | 3 | 4 | 5 | 6 | 7 *Strongly Agree* |
| Applicability | 18. The guideline describes facilitators and barriers to its application. | | | | | | | X |
| | 19. The guideline provides advice and/or tools on how the recommendations can be put into practice. | | | | | | | X |
| | 20. The potential resource implications of applying the recommendations have been considered. | | | | | | | X |
| | 21. The guideline presents monitoring and/ or auditing criteria. | | | | | | | X |
| Editorial independence | 22. The views of the funding body have not influenced the content of the guideline. | | | | | | | X |
| | 23. Competing interests of guideline development group members have been recorded and addressed. | | | | | | | X |
| Overall Guideline Assessment | 1. Rate the overall quality of this guideline. | 1 *Lowest possible quality* | 2 | 3 | 4 | 5 | 6 | 7 *Highest possible quality* |
| Overall Guideline Assessment | 2. I would recommend this guideline for use. | *Yes* | *Yes, with modifications* | | *No* | | | |
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# 11. References

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