Clinical guideline

NOAC / DOAC Apixaban (Eliquis®) EDOXABAN (Lixiana®) or Rivaroxaban (Xarelto®) MANAGEMENT OF HAEMORRHAGE AND/OR EMERGENCY

SETTING Trust-wide

FOR STAFF Medical staff

PATIENTS Adult patients requiring urgent surgical or invasive procedures who are taking Apixaban Edoxaban or Rivaroxaban

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NOTE:

- For Dabigatran (Pradaxa®) see separate guideline
- Please see related guideline - NOACs (Novel oral anticoagulants) Direct Oral Anticoagulants (DOACS) – a quick guide apixaban (eliquis®), dabigatran (pradaxa®), edoxaban (lixiana®) & rivaroxaban (Xarelto®)

Background

- Apixaban (Eliquis®) Edoxaban (Lixiana®) and Rivaroxaban (Xarelto®) are direct oral anticoagulants (DOACS) previously known as NOACs. They are direct inhibitors of Factor Xa and are currently used in prevention of thromboembolic stroke in selected patients with atrial fibrillation, prevention of venous thromboembolism in patients post hip and knee arthroplasty and treatment of venous thromboembolism (PE and DVT).
- Whilst the mechanism of action is the same there are some differences especially in dosing between the drugs.
- Patients on these drugs do not require routine monitoring but therapeutic doses may cause prolongation of standard clotting tests Prothrombin Time (PT), Activated Partial Thromboplastin Time (aPTT).
- Clotting times are affected less by Apixaban.
- Even at full therapeutic drug levels aPTT and PT may be normal so clotting screen should be interpreted with caution.
- Drug levels are available on ICE but may not be processed urgently (type in the drug name to the search engine). Correlation of bleeding risk with drug level is difficult.

Principles of managing emergency patient on Apixaban or Rivaroxaban

- There is currently no specific antidote onsite for Apixaban Edoxaban or Rivaroxaban
- Vitamin K and protamine will have NO EFFECT on bleeding risk associated with these drugs
- Fresh Frozen Plasma (FFP) is not recommended
- Clotting factor concentrates used to reduce bleeding include
  - **Prothrombin Complex Concentrate (Octaplex®)** Octaplex® guidance
  - Activated Prothrombin Complex Concentrate (FEIBA®)
  - Recombinant activated Factor Seven (Novoseven®)

All of these are associated with thrombotic risk and should only be used after discussion with a Haematologist.

Dosing will vary according to patient factors including thrombotic risk, current renal function, site of surgery and estimated time since last dose of anticoagulant.

- Due to high plasma protein binding haemodialysis will not be effective at removing these drugs
- If used within 2hrs of ingestion activated charcoal may be useful.
- All drugs reach full therapeutic effect within 2-3hrs of the dose
- For planned surgery it is recommended to stop at least 24 hours prior to surgery for both drugs. For planned major/critical site surgery they should be stopped at least 48hrs preop.
- The half-life of Apixaban is approximately 12 hours.
- The half-life of Edoxaban is approximately 10-14hrs
- The half-life of Rivaroxaban is approximately 7hrs (5-9hrs)

- **ASSESS PATIENT: Resuscitate.**
- Try and establish when last dose of drug was taken and document
- **Withhold Apixaban/Edoxaban/Rivaroxaban**
- **Urgent bloods:** (minimum required): FBC, renal function, clotting screen/fibrinogen, Rivaroxaban antiXa (if appropriate) (*interpret clotting screen with caution, normal values may be seen in the presence of full anticoagulant effect; a low fibrinogen is NOT due to the drug)*
- **Discuss with Haematology at an early stage if concerns** (On call bleep: [redacted], or via switch when out of hours)

Potentially clinically significant anticoagulant effect is **likely** to be present if last dose taken within 24-48hrs
Consider activated charcoal if ingestion <2 hours ago

Maintain BP and urine output

Is the patient actively bleeding?

Yes

No

Monitor.

See next page for surgery guidelines.

General measures: e.g. Mechanical compression/radiological intervention/endoscopy

Minor bleeding

Major Bleeding

Life threatening bleed

Bleeding remains mild or controlled?

No

Yes

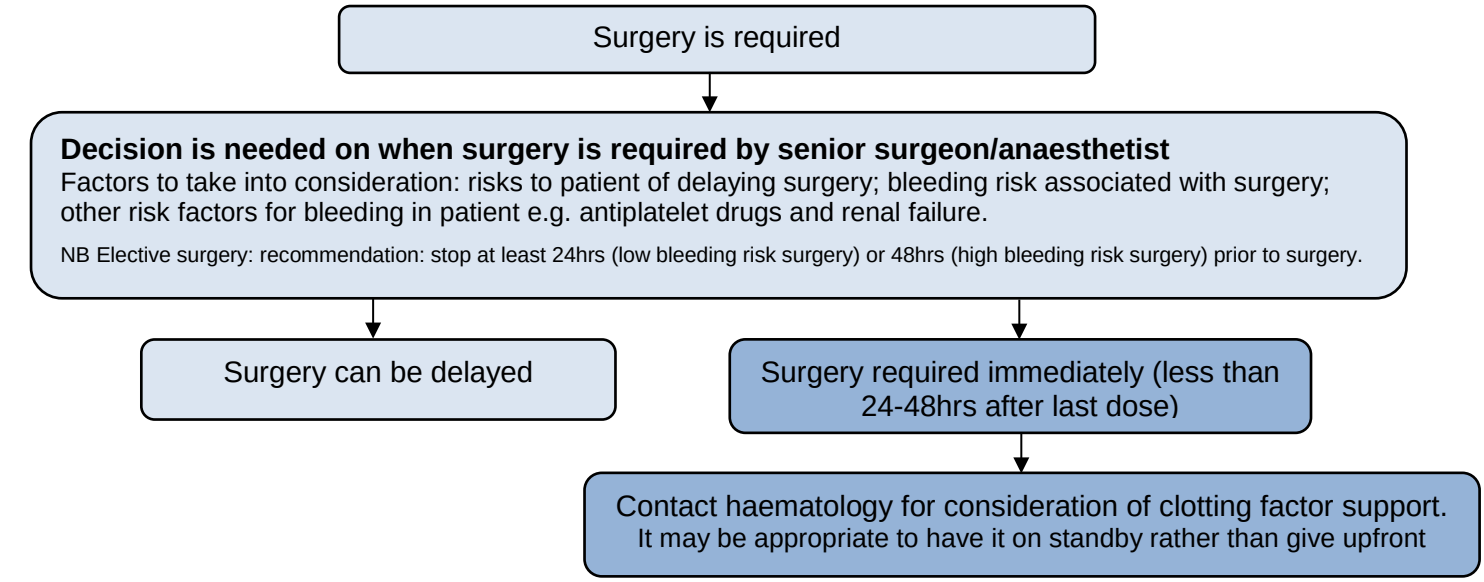
Delay next dose or discontinue.

See next page for surgery guidelines.

Consider Tranexamic acid 1g intravenously (avoid if renal tract bleeding)
Activate major haemorrhage protocol (as appropriate)
Supportive care aiming at maintaining
- Hb >7g/l
- Platelets >50x10^9/l (>100x10^9/l CNS bleeding)

Consider intervention to stop bleeding e.g. surgery/endoscopy
(All confirmed **<u>neurological bleeding</u>** should be discussed with Haematology & Neurosurgeons)

Discuss with Haematology SpR for consideration of clotting factor support PCC (Octaplex®) supply is in transfusion laboratory Bleep [redacted] or contact via UH Bristol switch if out of hours.



Regional anaesthesia: recommendation is to delay until 48hrs after last dose of Apixaban/Edoxaban/Rivaroxaban assuming renal function is normal and there are no other risk factors for bleeding. (a shorter time interval may be sufficient following a prophylactic dose depending on risk/benefit)

If surgery is delayed more than 48 hours from last dose of Apixaban/Edoxaban/Rivaroxaban patient should be VTE risk assessed regularly and given standard VTE thromboprophylaxis with low molecular weight heparin if appropriate - assuming scheduling of surgery is not a contraindication

Postoperative Management

Full dose anticoagulation should not be commenced until a minimum of 24-48 hours postoperatively.
Do not recommence drug until haemostasis secured.

Whilst an epidural is in situ anticoagulation is best managed with prophylactic low molecular weight heparin remembering that insertion and removal of the epidural catheter must be delayed by 12 hours after a prophylactic dose of Clexane and the dose of Clexane should be delayed by 4hrs after the removal of a catheter.

If drug inadvertently given which epidural catheter in situ do not remove epidural catheter less than 18-24hrs after last dose. Wait at least 6 hrs after catheter removal before next dose (24 hours if traumatic puncture)

Prophylactic anticoagulation may be required initially, especially if the patient is nil by mouth this may be best delivered using prophylactic low molecular weight heparin until the bleeding risk is satisfactory and/or the patient is able to tolerate oral medications

Table A

REFERENCES	**Makris, M., Veen, J. J., Tait, C. R., Mumford, A. D., & Laffan, M. (2013)**. Guideline on the management of bleeding in patients on antithrombotic agents. British journal of haematology, 160(1), 35-46. http://onlinelibrary.wiley.com/doi/10.1111/bjh.12107/pdf For summary product characteristics (SPCs) please see: https://www.medicines.org.uk/emc/
RELATED DOCUMENTS	Trust related documents: **NOACs DOACs: A Quick Guide For Indications/Dosing And Advice Regarding Elective Procedures** **NOACs DOACs Dabigatran Management of bleeding and/or emergency surgery** **Octaplex® Guidance**
AUTHORISING BODY	Thrombosis and Anticoagulation Committee
SAFETY	Contact Adult Haematology Registrar bleep [redacted] (out of hours contact on call Adult Haematology registrar on call via UHBristol switchboard)
QUERIES	Ward Pharmacist or Haematology Registrar as above