Apixaban: Bleeding, Surgery and Overdose - Full Clinical Guideline

Reference no.: CG-T/2014/212

1. Introduction

Apixaban is a Direct Oral Anticoagulant (DOAC) frequently prescribed for the prevention of stroke in non-valvular atrial fibrillation and treatment and secondary prevention of venous thromboembolism, as well as for other various indications which are outlined in the Trust's DOAC prescribing guideline. Bleeding is a recognised complication.

2. Aim and Purpose

This document describes how to manage bleeding, surgery and overdose in patients taking Apixaban; or who have taken an overdose of Apixaban.

3. Definitions, Keywords:

PT – Prothrombin Time; APTT – Activated Partial Thromboplastin Time; INR – International Normalized Ratio; eGFR – estimated Creatinine Clearance; FBC – Full Blood Count; LFT – Liver Function Tests; U&E - Urea and electrolytes

4. Pharmacokinetics and Interpretation of Coagulation Screen

- Apixaban has peak levels 3 - 4 hours after ingestion
- It has a half-life of approximately 12 hours
- Renal excretion of apixaban accounts for approximately 27% of total clearance
- Apixaban is **not** dialysed
- Apixaban prolongs PT and APTT although changes are small and subject to high variability
- Patients may have normal coagulation times despite therapeutic concentrations

5. Bleeding and Overdose

- **Stop apixaban**. Document the time of the last dose.
- If taken within 1 hour of a toxic dose (0.5mg/kg), consider activated charcoal (50g for adults)
- Optimise renal function
- Check FBC, LFTs, U&Es at presentation
- Check coagulation screen:
    - On presentation
    - At 6 hours after ingestion if previous screen is abnormal
    - Continue monitoring every 6-12 hours until coagulation is returning to normal

Note: PT and APTT may be normal despite increased bleeding risk.

- If patient has overdosed and is not actively bleeding, monitor coagulation screen as above. Reconsider the need for anticoagulation.
- Consider whether to delay next apixaban dose or discontinue treatment as appropriate.
    - Management should be individualised according to the severity and location of the bleed, as below:

Minor bleeding:
Local haemostatic measures (where possible).
Consider tranexamic acid orally (25 mg/kg TDS), IV (15mg/kg) and/or topically (e.g. mouthwash applied directly to a bleeding point). Delay next dose of apixaban, or discontinue.

Major bleeding:
Local haemostatic measures (where possible).
Give tranexamic acid IV (15 mg/kg) and/or topically (mouthwash applied directly to bleeding point).
Give fluid replacement
Give blood product support as indicated by Hb, other coagulopathy, platelets (if count< 75 x 109/L or antiplatelet agents).
Activate and follow the major haemorrhage alert if indicated.
In ongoing life or limb threatening bleeding: Consider use of Prothrombin Complex Concentrate (Octaplex, unlicensed use) 30 units/kg (discuss with Haematologist) - see separate Trust guidance for more details.
In life-threatening or uncontrolled bleeding in the gastrointestinal tract: consider Andexanet alfa (Ondexxya). Discuss with Haematologist for further advice and see separate Trust guideline for more details.
Note that there is lack of data to support the combined use of Andexanet alfa and Octaplex for the same bleeding episode.

There is currently very limited clinical experience with the use of PCC (Octaplex) in individuals receiving apixaban. The recommendation is based on limited non- clinical data.

6. Surgery/interventional radiology procedures

When interrupting DOAC therapy for surgery, the patient's renal function should be taken into consideration. See the Trust's DOAC prescribing guideline to establish that the patient is taking the correct dose of apixaban. Any patient where there is concern regarding the safe management of apixaban or with reduced renal function, particularly CrCl<15ml/min, seek advice from haematology.

Planned surgery/procedure: Omit apixaban before the procedure depending on the bleeding risk and renal function as below. Give thromboprophylaxis as usual. Restart Apixaban when haemostasis is secure.

Bleeding risk of procedure	**Number of doses to be omitted prior to procedure (including any doses due on the morning of surgery – Day 0)**		
	Day – 2	**Day –1**	**Day 0**
High	Omit 5 doses		
Low		Omit 3 doses	

Emergency surgery/procedure:

- **Stop apixaban**. Document the time of the last dose.
- If taken within 1 hour, consider activated charcoal (50g for adults)
- Optimise renal function.
- **Delay surgery/procedure if clinically possible.**
- If procedure cannot be delayed:
    - Local haemostatic measures (where possible).
    - Give tranexamic acid IV (15 mg/kg) and/or topically (mouthwash applied directly to bleeding point).

- Give fluid replacement.
- Give blood product support as indicated by Hb, other coagulopathy, platelets (if count< 75 x 10^9/L or antiplatelet agents).
- Consider use of Prothrombin Complex Concentrate (Octaplex, unlicensed use) 30units/kg (discuss with Haematologist).

Apixaban should be restarted after the surgical or other procedures as soon as adequate haemostasis has been established.

7. References

Apixaban (Eliquis) Summary of Product Characteristics (accessed October 2021)

Renal drug database (accessed October 2021)

Toxbase (Accessed October 2021)

The Handbook of Perioperative Medicines UKCPA (accessed October 2021)

8. Documentation Controls

Initial development of Guideline:	Dr A McKernan 2018
Consultation with:	Haematology thrombosis group Clinical Pharmacy Team
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Key Contact:	Dr A McKernan