University Hospitals of Derby and Burton NHS Foundation Trust

Rivaroxaban: Bleeding, Surgery and Overdose - Full Clinical Guideline

Reference no.: CG-T/2014/166

1. Introduction

Rivaroxaban 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 rivaroxaban; or who have taken an overdose of rivaroxaban

3. Definitions, Keywords:

PT – Prothrombin Time; APTT – Activated Partial Thromboplastin Time; INR – International Normalized Ratio**;** eGFR – estimated Glomerular Filtration Rate; FBC – Full Blood Count; LFT – Liver Function Tests; U&Es – Urea and electrolytes

4. Pharmacokinetics and Interpretation of Coagulation Screen

- Rivaroxaban has peak levels 2 - 4 hours after ingestion
- It has a half-life of approximately 5-9 hours (11-13 hours in elderly)
- Renal excretion of rivaroxaban accounts for approximately 33% of total clearance
- Rivaroxaban is **not** dialysed.
- Rivaroxaban 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 rivaroxaban**. Document the time of the last dose.
- **If a toxic dose has been taken (1mg/kg), consider giving activated charcoal (50g for adult)**. In patients with large overdoses (3mg/kg), give further doses of activated charcoal every 4 hours. Consider an antiemetic and review need for activated charcoal after 4 doses or sooner if clinical features resolve.
- 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.
- 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 rivaroxaban, 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 10^9/L or antiplatelet agents).
In ongoing life or limb threatening bleeding: Consider use of Prothrombin Complex Concentrate (Octaplex, unlicensed use) 30units/kg (discuss with Haematologist) – see separate Trust guidance for supply 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 further 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 rivaroxaban. 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 rivaroxaban. Any patient where there is concern regarding the safe management of rivaroxaban or with reduced renal function (particularly CrCl<15ml/min), seek advice from haematology.

Planned surgery/procedure:
Omit rivaroxaban before the procedure depending on bleeding risk and renal function as below. Give thromboprophylaxis as usual. Restart Rivaroxaban 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	Morning dose – omit 3 doses Evening dose – omit 2 doses		
Low	[redacted]	Morning dose – omit 2 doses Evening dose – omit 1 dose	

Note low dose rivaroxaban (2.5mg BD) is licensed for use in conjunction with aspirin +/- clopidogrel. Pre-operative cessation of low-dose rivaroxaban has not been studied and patients should be managed on a case-by-case basis. Discuss with cardiologist or vascular surgeon (depending on indication) for advice.

Emergency surgery/procedure:

- **Stop rivaroxaban**. Document the time of the last dose.
- 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)

7. References

Rivaroxaban (Bayer plc) Summary of Product Characteristics (accessed November 2021)

Renal drug database (accessed November 2021)

Toxbase (accessed November 2021)

The Handbook of Perioperative Medicines UKCPA (accessed November 2021)

8. Documentation Controls

Initial development of guideline:	A McKernan (2018)
Consultation with:	Thrombosis committee/haematology Clinical Pharmacy Team
Version No.	3
Modifications	November 2021, April 2022 (Rebecca Greenham – Advanced Pharmacist) Small modification to layout of guideline Addition of information of andexanet alfa use as a treatment option in life-threatening GI bleed.
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