

Edoxaban: Bleeding, Surgery and Overdose - Full Clinical Guideline

Reference no.: CG-T/2014/212

1. Introduction

Edoxaban is a Direct Oral Anticoagulant (DOAC) frequently prescribed for the prevention of stroke in non-valvular atrial fibrillation 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 and surgery in patients taking Edoxaban, or who have taken an overdose of Edoxaban.

3. Definitions, Keywords: PT – Prothrombin Time; APTT – Activated Partial Thromboplastin Time; INR – International Normalized Ratio; CrCl – Creatinine Clearance; FBC – Full Blood Count; LFTs – Liver Function Tests; PCC; prothrombin complex concentrate; U&Es – Urea and Electrolytes

4. Pharmacokinetics and Interpretation of the Coagulation Screen

- Edoxaban has peak levels 1-2 hours after ingestion.
- It has a half-life of approximately 10-14 hours.
- It is 35% renally excreted.
- Edoxaban **is not** dialysable except only 9% via haemodialysis.
- Edoxaban may prolong PT and APTT assays with differing sensitivity. Patients may have normal coagulation times despite therapeutic concentrations.

5. Bleeding and Overdose

- **There is no antidote to edoxaban.**
- **Stop edoxaban.** Document the time of the last dose.
- If taken within 1 hour at a toxic dose (3mg/kg), consider activated charcoal (50g for adults).
- Optimise renal function
- Request FBC, LFTs, U&Es and coagulation screen:
 - At presentation
 - Repeat coagulation screen at 6 hours after ingestion if the screen is abnormal.
 - Repeat every 6-12 hours until coagulation is returning to normal.
- If patient has overdosed and is not actively bleeding, monitor coagulation screen as above. Reconsider the need for anticoagulation.
 - Consider whether to delay next edoxaban 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 edoxaban, 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 concomitant 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)

There is currently very limited clinical experience with the use of antifibrinolytic agents (tranexamic acid) and PCC (Octaplex). The recommendation is based on limited non-clinical data.

Protamine sulfate and vitamin K are not expected to affect the anticoagulant activity of edoxaban.

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 edoxaban. Any patient where there is concern regarding the safe management of edoxaban or with reduced renal function, particularly CrCl < 30ml/min, seek advice from haematology.

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

Bleeding Risk of Procedure	Time of day patient usually takes edoxaban (once daily dosing)	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	Omit	Omit	Omit
	Evening	Omit	Omit	
Low	Morning		Omit	Omit
	Evening		Omit	

Emergency surgery/procedure:

- **There is no antidote to edoxaban**
- **Stop edoxaban.** Document the time of the last dose.
- Optimise renal function
- If taken within 1 hour, consider activated charcoal (50g for adults)
- **Delay surgery/procedure if clinically possible**, if not:
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).
Consider use of Prothrombin Complex Concentrate (Octaplex, unlicensed use) 30units/kg (discuss with Haematologist)

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

7. References.

UKCPA Handbook of Peri-operative Medicines (Accessed May 2021)

Toxbase (Accessed May 2021)

Edoxaban tosilate (Lixiana) Summary of Product Characteristics – Daiichi Sankyo (Last Updated 12 Jan 2021)

Renal drug database (Accessed May 2021)

8. Documentation Controls

Initial development of Guideline:	Rebecca Greenham (Advanced Clinical Pharmacist) 2021
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Key Contact:	Rebecca Greenham rebecca.greenham1@nhs.net