Clinical Guideline

ANDEXANET ALFA GUIDELINE

SETTING	Trust-wide
FOR STAFF	Medical staff
PATIENTS	Adult patients taking rivaroxaban or apixaban with life-threatening or uncontrolled gastrointestinal bleeding.

NOTE:

For advice on non-gastrointestinal haemorrhage for patients on apixaban (Eliquis®), edoxaban (Lixiana®), rivaroxaban (Xarelto®) see separate guideline.

Direct Oral Anticoagulants (DOACS) – a quick guide apixaban (Eliquis®), dabigatran (Pradaxa®) & rivaroxaban (Xarelto®) see guideline.

Background

Andexanet alfa is recommended by NICE [TA697] as an option for reversing anticoagulation from apixaban or rivaroxaban in adults with life-threatening or uncontrolled gastrointestinal bleeding. Andexanet binds to Factor (FXa) inhibitors and allows restoration of native FXa activity, thus increasing thrombin generation. It should not compete with native FXa for incorporation into the prothrombinase complex.
After binding, andexanet dissociates from the FXa inhibitor and both agents are eliminated. The elimination half-life of andexanet ranges from four to seven hours.

Safety and efficacy

The effectiveness of andexanet alfa for non-gastrointestinal bleeding has not been demonstrated and therefore andexanet alfa should not be used for other types of major bleeding. There is no evidence directly comparing andexanet alfa with established clinical management (including prothrombin complex concentrate) and the indirect comparison has limitations. There is a risk of thrombotic complications associated with use of andexanet alfa which needs to also be considered.

Considerations for use of Andexanet Alfa:

1. ***Initial assessment of the patient is vital to review whether a clinically relevant concentration of apixaban or rivaroxaban is expected to be present:***

    - What dose is the patient taking?
    - When was the most recent dose taken?
    - What is the patient's renal function?
    - Take bloods including clotting screen and drug level **(latter may not be able to be processed urgently and should not delay management)**

Andexanet alfa may not be appropriate for the following patients:

- Taking a low dose DOAC, particularly if >12h since last dose (apixaban 2.5mg twice daily, rivaroxaban 10mg once daily or rivaroxaban 2.5mg twice daily).
- Patients who have received a therapeutic dose >18h ago and CrCl >30mls/min (these patients weren't included in the trial).
- Beyond 24h after administration, rivaroxaban and apixaban levels are expected to be very low.

2. Assessment of bleeding severity

Andexanet alfa is only indicated in patients with acute major bleeding from the gastrointestinal tract, with one or more of the following features:

- Potentially **life-threatening bleeding with signs or symptoms of haemodynamic compromise** (e.g., severe hypotension, poor skin perfusion, mental confusion, or low cardiac output that could not otherwise be explained)
- Bleeding associated with a **decrease in the haemoglobin level of at least 20 g/l** (or a haemoglobin level of ≤80 g/l if no baseline haemoglobin level is available)

Andexanet alfa is kept in the Emergency Department Majors fridge.

Please contact the Haematology Registrar or Haemostasis consultant on call for advice prior to administration.

Dosing and administration:

Please see Medusa or SPC for more details on administration

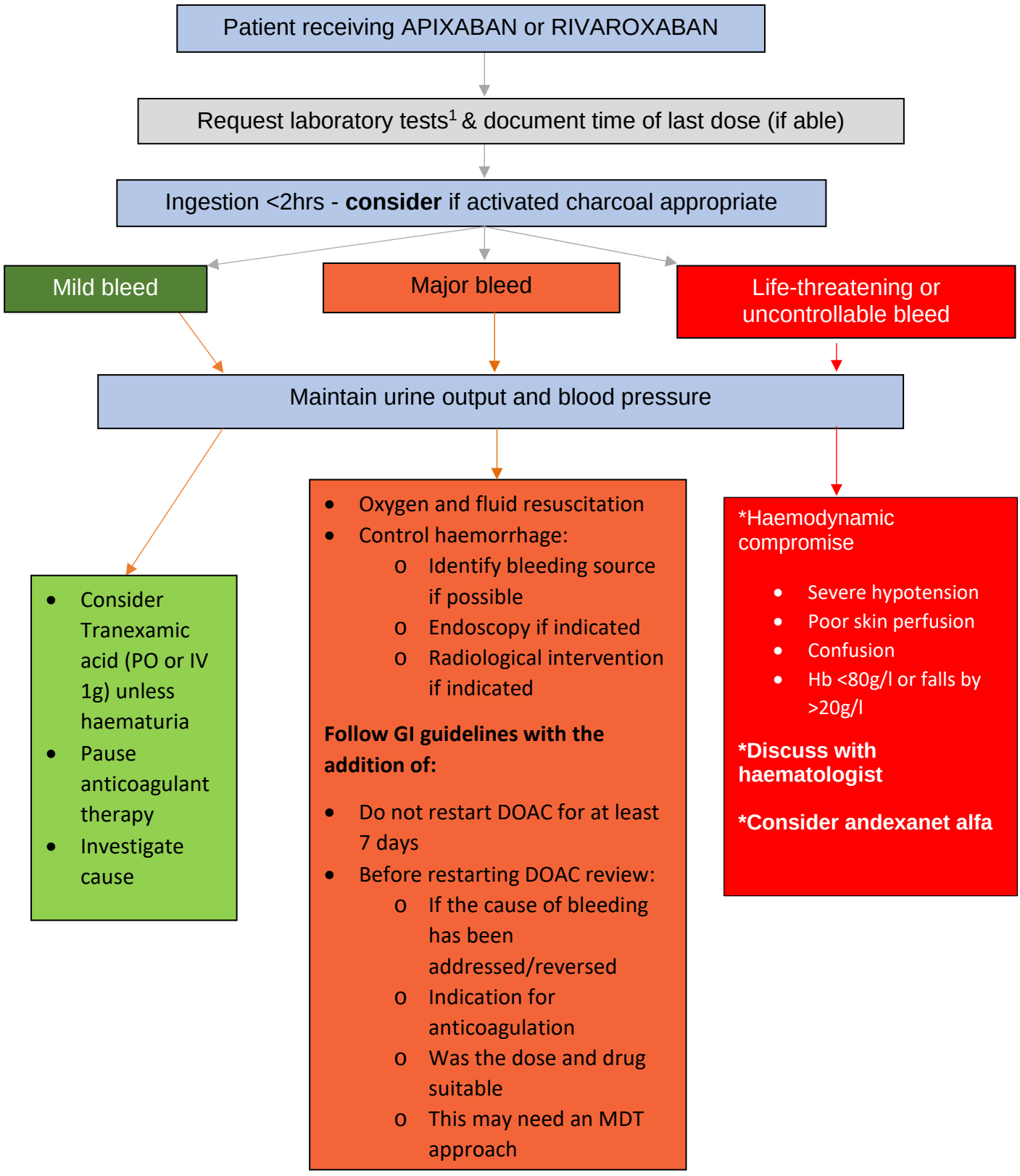
Andexanet dosing depends on the specific DOAC, the dose and time since last dose taken. (see table 1).

Table 1:

DOSE	INITIAL IV BOLUS	FOLLOW ON INFUSION	NUMBER OF VIALS NEEDED
Low dose	400mg bolus at a rate of 30mg/minute	Rate 4mg/minute for 120 minutes (480mg)	5 x 200mg total
High dose	800mg bolus at a rate of 30mg/minute	Rate 8mg/minute for 120 minutes (960mg)	9 x 200mg total

DOAC TO BE REVERSED	DOSE OF DOAC	TIMING OF LAST DOAC DOSE <8 HOURS	TIMING OF LAST DOAC DOSE ≥ 8 HOURS
Rivaroxaban	≤10mg	Low dose	Low dose
	>10 mg or unknown	High dose	
Apixaban	≤ 5 mg	Low dose	Low dose
	>5mg or unknown	High dose	

Figure 1: Haemorrhage pathway – management of patients anticoagulated with rivaroxaban or apixaban with gastrointestinal bleeding



1. To include Group and save (x2 if no historical group), FBC, full coagulation screen (PT, APTT, fibrinogen) and consider DOAC level if using Andexanet alfa – this may not be processed urgently – do NOT wait for the results unless agreed with on call haematologist

REFERENCES	Overview | Andexanet alfa for reversing anticoagulation from apixaban or rivaroxaban | Guidance | NICE For summary product characteristics (SPCs) please see: https://www.medicines.org.uk/emc/product/10933 [redacted], [redacted], [redacted], [redacted], [redacted], [redacted] et al. Full study report of andexanet alfa for bleeding associated with Factor Xa inhibitors. The New England journal of medicine. 2019. Ondexxya® Andexanet alfa Formulary Information Pack November 2019 PP-AnXa-UK-PR2019001 Ondexxya® Andexanet alfa Clinical protocol March 2021 UK/POR-ODX/0004 https://bnf.nice.org.uk/drug/andexanet-alfa.html
RELATED DOCUMENTS AND PAGES	Noac Apixaban Eliquis Or Rivaroxaban Xarelto Management Of Haemorrhage And Or Emergency Surgery Noacs Doacs A Quick Guide Apixaban Eliquis Dabigatran Pradaxa And Rivaroxaban Xarelto
AUTHORISING BODY	Haematology governance
SAFETY	Contact Adult Haematology Registrar bleep [redacted] (out of hours contact on call Adult Haematology registrar on call via UH Bristol switchboard)
QUERIES AND CONTACT	Ward pharmacists or Haematology Registrar as above.