# ANTICOAGULATION REVERSAL

Warfarin · DOACs · Heparin · major bleeding

**STOP THE** *bleed*

## EVERY MAJOR BLEED · DO THIS FIRST

### STABILISE

ABC; direct pressure / packing. Urgent surgery, endoscopy or interventional radiology for the source.

### TRANSFUSE

To targets: platelets > 50 (>100 if CNS), fibrinogen > 1.5 g/L, correct $Ca^{2+}$ & temp. Give TXA 1 g.

### ASSESS

Which drug, what dose, time of last dose, renal & hepatic function. Send a drug-specific assay.

## DOAC REVERSAL

*specific agent first; PCC if unavailable*

| DOAC | Specific reversal | Dose | If unavailable |
|---|---|---|---|
| **Dabigatran** | Idarucizumab | 5 g IV (2 × 2.5 g) | 4F-PCC 50 U/kg; haemodialysis |
| **Apixaban** | Andexanet alfa | low- or high-dose by dose & timing | 4F-PCC 50 U/kg |
| **Rivaroxaban** | Andexanet alfa | low- or high-dose by dose & timing | 4F-PCC 50 U/kg |
| **Edoxaban** | (andexanet not licensed) | - | 4F-PCC 50 U/kg |

**Andexanet dose:** LOW = 400 mg bolus + 480 mg over 2 h (last dose > 8 h, or ≤ apixaban 5 mg / rivaroxaban 10 mg); HIGH = 800 mg + 960 mg otherwise.

**ANNEXA-I (2024):** *andexanet cut haematoma expansion but raised thrombotic events - weigh carefully and restart anticoagulation when safe.*

## WARFARIN (vit-K antagonist)

- **Life-threatening bleed -** 4F-PCC 25-50 U/kg (by INR & weight) + IV vitamin K 5-10 mg
- **INR high, no bleed -** hold warfarin ± oral vitamin K 1-5 mg
- **FFP -** only if PCC unavailable (slow, volume load)

## HEPARINS

- **Unfractionated (UFH) -** protamine 1 mg per 100 units given in the last 2-3 h (max 50 mg)
- **LMWH (enoxaparin) -** protamine 1 mg per 1 mg if < 8 h; only ~60-75% reversal
- **Fondaparinux -** no antidote; consider aPCC / rFVIIa in extremis

## LABS & TIMING

- Last dose + renal function (CrCl) predict the drug effect
- Anti-Xa (drug-calibrated): apixaban, rivaroxaban, LMWH
- Dilute thrombin time / ecarin: dabigatran
- A normal PT / aPTT does NOT exclude a DOAC effect

## WHEN TO REVERSE

- Life-threatening or critical-site bleed (intracranial, spinal, pericardial, airway)
- Major haemorrhage uncontrolled despite local measures
- Emergency surgery that cannot be delayed
- NOT for minor bleeding - hold the drug + supportive care

## ANTIPLATELET AGENTS

- **Platelet transfusion -** limited benefit; AVOID routine in spontaneous ICH (PATCH) - reserve for surgery / severe bleed
- **Desmopressin -** DDAVP 0.3 mcg/kg may improve platelet function
- **Ticagrelor -** no licensed reversal (bentracimab investigational)

## AFTER REVERSAL · RESTART

- Reassess bleeding vs thrombotic risk daily
- Restart anticoagulation once haemostasis is secured (individualise; often 1-2 weeks after ICH)
- Mechanical VTE prophylaxis first; add drug cover when safe

## PEARLS & PITFALLS

- A normal PT / aPTT does not exclude a DOAC - use drug-specific assays and the last-dose time.
- Andexanet and PCC are prothrombotic - reverse only life-threatening bleeds and restart anticoagulation when safe.
- Reversal agents are adjuncts: give TXA, transfuse to targets and control the source.
- Idarucizumab rapidly and completely reverses dabigatran, which is also removed by dialysis.

**References:** ISTH DOAC Reversal 2024 · Neurocritical Care / SCCM 2016 · ANNEXA-4 2019 & ANNEXA-I 2024.

*Educational aid; verify doses against local protocol and patient factors.*