ICR-ACR-040

Critical care · hemostasis

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CRITICAL CARE EMERGENCY PROTOCOL

Anticoagulation Reversal

Reversal of anticoagulants and antiplatelets in active bleeding. Identify the agent and time of last dose, judge whether bleeding is life-threatening, give the right antidote, and control the source. Match every reversal to the specific drug — the wrong agent wastes the minutes that matter. Adapt all doses to your formulary and local policy.

ALL General notes — apply to every patient

FIRST MOVES **Hold all further anticoagulant doses** · achieve mechanical / surgical hemostasis where possible · **avoid intramuscular injections**.

CHECK & ORDER — LABS

- [ ] PT/INR, aPTT
- [ ] CBC, fibrinogen
- [ ] Type & crossmatch
- [ ] Creatinine, LFTs

ASSESS

- [ ] **Time of last dose** & agent
- [ ] Indication (mechanical valve, VTE, AF) — thrombotic risk of reversal
- [ ] Weight & renal function
- [ ] **Severity / site** — life-threatening vs non–life-threatening

JUMP TO Identify the class, then go to its section — **01** Warfarin · **02** UFH · **03** LMWH · **04** Direct thrombin inhibitors · **05** Factor Xa inhibitors · **06** Fondaparinux · **07** Antiplatelets · **08** Supportive · **09** Documentation.

01 Warfarin (vitamin K antagonist)

LABS / MONITORING

- [ ] **PT/INR STAT** and **q6–8h** until stable; CBC, fibrinogen; type & crossmatch

A · Life-threatening / critical bleeding (ICH, massive GI bleed)

- [ ] **Hold warfarin**
- [ ] **4-factor PCC** (Kcentra) — fixed: **`1500–2000 units IV once`** (common ICH protocol), OR INR-based below

INR 2–<4	`25 units/kg IV`	max 2500
INR 4–6	`35 units/kg IV`	max 3500
INR > 6	`50 units/kg IV`	max 5000

- [ ] **Vitamin K (phytonadione) 10 mg IV once**, slow over 30 min
- [ ] **If PCC unavailable — FFP** `10–15 mL/kg IV` (≈ 3–4 units); watch volume status

B · Serious, non–life-threatening

- [ ] **Vitamin K 2.5–5 mg IV or PO once**
- [ ] Consider PCC if clinically significant (dose as in A)

C · No bleeding, ↑ INR

- [ ] **INR 4.5–10** — hold warfarin; vit K usually not needed (1–2.5 mg PO if high bleed risk)
- [ ] **INR > 10** — vit K 2.5–5 mg PO once + hold; recheck INR

02 Unfractionated heparin (IV or SC)

LABS / MONITORING

- [ ] aPTT, anti-Xa (if used), platelets (**HIT** risk), CBC

A · Serious / life-threatening bleeding

- [ ] **Hold heparin** infusion / injections
- [ ] **Protamine sulfate IV** — **`1 mg per 100 units`** heparin given in prior 2 h (**max 50 mg/dose**)
- [ ] Dilute in 50–100 mL NS, infuse over 10–15 min (**`≤ 5 mg/min`**) to limit hypotension / anaphylactoid reaction
- [ ] Repeat **`0.5 mg per 100 units`** if aPTT remains prolonged or bleeding persists

B · Non–life-threatening bleeding

- [ ] Often just **stop heparin** — effect dissipates within hours (short half-life). Protamine still an option for more significant bleeding (as in A)

03 Low-molecular-weight heparin (enoxaparin)

PARTIAL ONLY Protamine reversal of LMWH is **incomplete**. Labs — CBC, anti-Xa (if available), creatinine.

A · Therapeutic-dose LMWH + serious bleeding

- [ ] **Hold LMWH**
- [ ] **Within 8 h** of last dose — protamine `1 mg per 1 mg enoxaparin` (or per 100 units anti-Xa)
- [ ] **8–12 h** since last dose — protamine `0.5 mg per 1 mg enoxaparin`
- [ ] **Max 50 mg/dose**, over 10–15 min; may repeat once at 0.5 mg per 1 mg if bleeding continues

B · Prophylactic-dose LMWH + significant bleeding

- [ ] Consider protamine `0.5–1 mg per 1 mg enoxaparin` given in last 8 h

04 Direct thrombin inhibitors

A · DABIGATRAN

- [ ] Labs — aPTT, thrombin time (or dilute TT), creatinine; anti-IIa level if available

Life-threatening / critical bleeding

- [ ] **Hold dabigatran**
- [ ] **Idarucizumab (Praxbind) 5 g IV total** — two `2.5 g` IV boluses over 5–10 min, back-to-back
- [ ] **If idarucizumab unavailable** — 4F-PCC `50 units/kg IV` (max ~5000) off-label rescue
- [ ] **Activated charcoal 50 g PO/NG** if ingestion < 2–4 h & airway protected; **hemodialysis** removes dabigatran

- [ ] **Non–life-threatening** — hold drug; local measures & transfusion support; hematology input before idarucizumab

B · Argatroban / bivalirudin (IV)

- [ ] **Short half-lives** — hold infusion, support hemostasis. No specific antidote; consider **hemodialysis for bivalirudin** in some settings (not argatroban)

05 Direct oral factor Xa inhibitors

Rivaroxaban, apixaban, edoxaban, betrixaban. Labs — PT/INR & aPTT (nonlinear), anti-Xa level if available, creatinine, LFTs.

A · Life-threatening / critical bleeding

- [ ] **Hold DOAC.** Preferred specific reversal — **andexanet alfa (Andexxa)**, dose by last dose & time since:

Low-dose

Apix ≤ 5 mg / riva ≤ 10 mg **and** ≥ 8 h ago (or unknown) → `400 mg IV bolus` over ~15 min, then `4 mg/min × 120 min` (total 480 mg)

High-dose

Apix > 5 mg / riva > 10 mg, **or** < 8 h / unknown → `800 mg IV bolus` over ~15 min, then `8 mg/min × 120 min` (total 960 mg)

- [ ] **If andexanet unavailable (common)** — 4F-PCC `50 units/kg IV` (max 5000) single dose
- [ ] **Activated charcoal 50 g PO/NG** if ingestion < 2–4 h (riva / apix)

B · Non–life-threatening bleeding

- [ ] Hold DOAC; local measures, blood products as indicated. Lower threshold for PCC if high-risk / expanding hematoma — consult hematology / neurosurgery / GI

06 Fondaparinux

NO ANTIDOTE **Protamine does not reliably reverse** fondaparinux.

- [ ] **Hold fondaparinux**

- [ ] Serious bleeding — consider **4F-PCC 50 units/kg IV** (off-label)
- [ ] Mechanical / operative control, supportive care, RBCs & platelets if indicated

07 Antiplatelet agents

Aspirin, clopidogrel, ticagrelor, prasugrel — not anticoagulants, but managed in the same order set. Labs — CBC, PT/INR, aPTT; platelet-function testing if rapidly available (optional).

Life-threatening bleeding or emergent surgery

- [ ] **Hold antiplatelet agents**
- [ ] **Platelet transfusion** — 1 apheresis unit IV, repeat by bleeding / platelet function. **Less effective with ticagrelor** (active drug in plasma)
- [ ] **DDAVP 0.3 mcg/kg IV** in 50 mL NS over 15–30 min (esp. uremia, aspirin/clopidogrel-related, ICH)
- [ ] **TXA 1 g IV over 10 min, then 1 g over 8 h** (if no thrombotic contraindication; trauma / ICH protocols)

08 Additional supportive orders

TRANSFUSION TARGETS

- [ ] RBCs to institutionally appropriate Hgb target
- [ ] Platelets ≥ `50,000/µL` for active major bleeding · ≥ `100,000/µL` for ICH / neurosurgery
- [ ] Cryoprecipitate / fibrinogen concentrate to **fibrinogen > 150–200 mg/dL** in major bleeding

ADJUNCT MEDICATIONS

- [ ] Suspected upper GI bleed — **pantoprazole 80 mg IV bolus, then 8 mg/h** infusion
- [ ] Antifibrinolytic — **TXA** as above in trauma / ICH where protocol indicates

09 Documentation & consults

DOCUMENT

CONSULTS TO CONSIDER

- Indication for reversal
- Timing & doses of all reversal agents
- Risk–benefit discussion if high thrombotic-risk indication

- Hematology
- Neurosurgery (ICH)
- GI (GI bleed)
- Interventional radiology / surgery for source control

EDUCATIONAL USE ONLY

Not a substitute for clinical judgement. Verify the agent, time of last dose, doses, allergies, renal/hepatic function, and contraindications. Weigh thrombotic risk of reversal. Adapt all agents and doses to your institutional formulary and policy.

Spreading knowledge
Improving outcomes