European Society of Anaesthesiology and Intensive Care

Patients with non-life threatening bleeding

History

Verify intake of direct FXa-inhibitors or direct thrombin inhibitor and **Direct evidence** by lab tests (e.g. calibrated anti-FXa-activity or (diluted) thrombin time for dabigatran).
Check for concomitant bleeding disorders or intake of platelet inhibitors.

Seek advice from thrombosis and haemostasis service

Blood sampling

PT, PT-ratio, aPTT, thrombin time (for dabigatran), calibrated anti-FXa-activity, point of care coagulation monitoring (if available), creatinine (GFR), fibrinogen, D-dimers and platelet count on admission to the hospital.

Important

Draw blood samples before treatment, but treatment should not be delayed by waiting for lab results.

YES
Apixaban, rivaroxaban

1. Consider "wait and see" strategy if clinically appropriate;
2. Andexanet alfa or PCC
3. aPCC if both drugs unavailable. Stimulate diuresis.

Consider **Standard Treatment** in addition

YES
Dabigatran

1. Consider "wait and see" strategy if clinically appropriate;
2. Idarucizumab.
3. PCC or aPCC if idarucizumb unavailable. Stimulate diuresis.

Consider **Standard Treatment** in addition

YES
Edoxaban*

*Andexanet alfa not approved as of June 2023

1. Consider "wait and see" strategy if clinically appropriate;
2. PCC
3. aPCC if PCC not available. Stimulate diuresis.

Consider **Standard Treatment** in addition

Clinical practice statements

In case of progression to severe or life-threatening bleeding: rule out surgical source of bleeding; continue standard treatment; consider a second antidote dose or PCC/aPCC dose if there are persistently elevated DOAC levels.
Recurrent bleeding: consider that elevated plasma levels of apixaban, rivaroxaban and dabigatran may occur after specific antidote application.
Terminated bleeding (e.g.>24–48h: consider resumption of anticoagulation e.g. LMWH at prophylactic dosage or local standard.

Standard treatment, e.g.:

Tranexamic acid, clotting factor concentrate, cryoprecipitate, platelet concentrate, desmopressin, if von Willebrand disease or aspirin-induced platelet disorder is verified/suspected.
Fresh frozen plasma in case of massive transfusion.

European Society of Anaesthesiology and Intensive Care

Patients with non-life threatening bleeding

Anticoagulant	Antidote	Non specific haemostatic agent
Dabigatran	Idarucizumab 2×2,5 g over 5–10 minutes, infusions no more than 10 minutes apart.	Not approved: PCC or aPCC at a dose of 25–50 IU/kg; rFVIIa: no recommendation
Apixaban	Low dose: 400 mg bolus over 15 minutes followed by an 480 mg infusion over 2h High dose: 800 mg bolus over 30 minutes followed by an 960mg infusion over 2h	Not approved: PCC or aPCC at a dose of 25–50 IU/kg; rFVIIa: no recommendation
Edoxaban	Not approved	Not approved: PCC or aPCC at a dose of 25–50 IU/kg; rFVIIa: no recommendation
Rivaroxaban	Low dose: 400 mg bolus over 15 minutes followed by an 480 mg infusion over 2h High dose: 800 mg bolus over 30 minutes followed by an 960mg infusion over 2h	Not approved: PCC or aPCC at a dose of 25–50 IU/kg; rFVIIa: no recommendation

European Society of Anaesthesiology and Intensive Care

Patients with confirmed intake of DOACs before urgent surgery

History

Verify intake of direct FXa-inhibitors or direct thrombin inhibitor and **Direct evidence** by lab tests (e.g. calibrated anti-FXa-activity or (diluted) thrombin time for dabigatran).
Check for concomitant bleeding disorders or intake of platelet inhibitors.

Seek advice from thrombosis and haemostasis service

Blood sampling

PT, PT-ratio, aPTT, thrombin time (for dabigatran), calibrated anti-FXa-activity, point of care coagulation monitoring (if available), creatinine (GFR), fibrinogen, D-dimers and platelet count on admission.

Important

Draw blood samples before treatment, but treatment must not be delayed by waiting for lab results.

YES
Apixaban, rivaroxaban

1. Consider „wait and see" strategy if clinically appropriate;
2. Andexanet alfa or PCC
3. aPCC if both drugs unavailable. Stimulate diuresis.

YES
Dabigatran

1. Consider „wait and see" strategy if clinically appropriate;
2. Idarucizumab.
3. PCC or aPCC if idarucizumb unavailable. Stimulate diuresis.

YES
Edoxaban*

*Andexanet alfa not approved as of June 2023

1. Consider „wait and see" strategy if clinically appropriate;
2. PCC
3. aPCC if PCC not available. Stimulate diuresis.

Clinical practice statements

In case of progression to severe or life-threatening bleeding: rule out surgical source of bleeding; continue standard treatment; consider a second antidote dose or PCC/aPCC dose if there are persistently elevated DOAC levels.
Recurrent bleeding: consider that elevated plasma levels of apixaban, rivaroxaban and dabigatran may occur after specific antidote application.
Terminated bleeding (e.g.>24–48h: consider resumption of anticoagulation e.g. LMWH at prophylactic dosage or local standard.

Standard treatment, e.g.:

Tranexamic acid, clotting factor concentrate, cryoprecipitate, platelet concentrate, desmopressin, if von Willebrand disease or aspirin-induced platelet disorder is verified/suspected.
Fresh frozen plasma in case of massive transfusion.

European Society of Anaesthesiology and Intensive Care

Patients with confirmed intake of DOACs before urgent surgery

Anticoagulant	Antidote	Non specific haemostatic agent
Dabigatran	Idarucizumab 2×2,5 g over 5–10 minutes, infusions no more than 10 minutes apart.	Not approved: PCC or aPCC at a dose of 25–50 IU/kg; rFVIIa: no recommendation
Apixaban	Low dose: Andexanet alfa 400mg bolus over 15 minutes followed by a 480mg infusion over 2h High dose: Andexanet alfa 800 mg bolus over 30 minutes followed by a 960 mg infusion over 2 hours	Not approved: PCC or aPCC at a dose of 25–50 IU/kg; rFVIIa: no recommendation
Edoxaban	Andexanet alfa not approved as of June 2023.	Not approved: PCC or aPCC at a dose of 25–50 IU/kg; rFVIIa: no recommendation
Rivaroxaban	Low dose: Andexanet alfa 400mg bolus over 15 minutes followed by a 480mg infusion over 2h High dose: Andexanet alfa 800 mg bolus over 30 minutes followed by a 960 mg infusion over 2 hours	Not approved: PCC or aPCC at a dose of 25–50 IU/kg; rFVIIa: no recommendation

European Society of Anaesthesiology and Intensive Care

Severe (haemodynamically unstable) or life-threatening bleeding (intracerebral, epidural, intraspinal, gastrointestinal, traumatic or other refractory bleeds)

History

Verify intake of direct FXa-inhibitors or direct thrombin inhibitor and
Direct evidence by lab tests (e.g. calibrated anti-FXa-activity or (diluted) thrombin time for dabigatran).
Check for concomitant bleeding disorders or intake of platelet inhibitors and exclude severe bleeding with an expected poor outcome

Maintain „adequate" BP levels (e.g., in trauma: syst. at 80–90 mmHg, in TBI/ICH > mean arterial BP of 80–90 mmHg)*; seek advice from thrombosis and haemostasis service

Blood sampling

PT, PT-ratio, aPTT, (diluted) thrombin time for dabigatran, calibrated anti-FXa-activity, point of care coagulation monitoring (if available), creatinine (GFR), fibrinogen, D-dimers, platelet count.

Important

Draw blood samples before treatment, but treatment should not be delayed by waiting for lab results.

YES
Apixaban, rivaroxaban

1. Andexanet alfa or PCC.
2. aPCC if both drugs unavailable.

Consider **Standard Treatment** in addition

YES
Dabigatran

1. Idarucizumab.
2. PCC or aPCC if idarucizumb unavailable.

Consider **Standard Treatment** in addition

YES
Edoxaban*

*Andexanet alfa not approved as of June 2023

1. PCC.
2. aPCC if PCC not available.

Consider **Standard Treatment** in addition

None

Standard treatment, e.g.:

Tranexamic acid, clotting factor concentrate, cryoprecipitate, platelet concentrate, desmopressin, if von Willebrand disease or aspirin-induced platelet disorder is verified/suspected.
Fresh frozen plasma in case of massive transfusion.

Clinical practice statements

In case of progression to severe or life-threatening bleeding: rule out surgical source of bleeding; continue standard treatment; consider a second antidote dose or PCC/aPCC dose if there are persistently elevated DOAC levels.
Recurrent bleeding: consider that elevated plasma levels of apixaban, rivaroxaban and dabigatran may occur after specific antidote application.
Terminated bleeding (e.g.>24–48h: consider resumption of anticoagulation e.g. LMWH at prophylactic dosage or local standard.

*: Rossaint R, Afshari A, Bouillon B, et al. The European guideline on management of major bleeding and coagulopathy following trauma: sixth edition. Crit Care. 2023;27(1):1–45. doi:10.1186/s13054–023–04327–7

European Society of Anaesthesiology and Intensive Care

Severe (haemodynamically unstable) or life-threatening bleeding (intracerebral, epidural, intraspinal, gastrointestinal, traumatic or other refractory bleeds)

Anticoagulant	Antidote	Non specific haemostatic agent
Dabigatran	Idarucizumab 2×2,5 g over 5–10 minutes, infusions no more than 10 minutes apart.	Not approved: PCC or aPCC at a dose of 25–50 IU/kg; rFVIIa: no recommendation
Apixaban	Low dose: Andexanet alfa 400mg bolus over 15 minutes followed by a 480mg infusion over 2h High dose: Andexanet alfa 800 mg bolus over 30 minutes followed by a 960 mg infusion over 2 hours	Not approved: PCC or aPCC at a dose of 25–50 IU/kg; rFVIIa: no recommendation
Edoxaban	Andexanet alfa not approved as of June 2023.	Not approved: PCC or aPCC at a dose of 25–50 IU/kg; rFVIIa: no recommendation
Rivaroxaban	Low dose: Andexanet alfa 400mg bolus over 15 minutes followed by a 480mg infusion over 2h High dose: Andexanet alfa 800 mg bolus over 30 minutes followed by a 960 mg infusion over 2 hours	Not approved: PCC or aPCC at a dose of 25–50 IU/kg; rFVIIa: no recommendation