Anticoagulation FORUM

# Order Set:
# Reversal & Hemostatic Therapies for DOAC-related, Life-Threatening Bleeding

Direct-acting oral anticoagulants (DOACs) are used widely for prevention and treatment of thromboembolism and consequently, clinicians are likely to encounter patients who present with life-threatening bleeding in the setting of DOAC use. The Anticoagulation Forum (AC Forum) created this Order Set template on reversal and hemostatic therapies for adults with DOAC-related, life-threatening bleeding to guide institutions in the creation, implementation, and maintenance of order sets. Our aim is to streamline care once anticoagulation reversal is deemed appropriate and is not intended to serve as a clinical decision tool to classify the severity of bleeding, nor to determine whether reversal is necessary. The authors acknowledge the lack of randomized trial data and, as such, this order set should be implemented with consideration of local formulary approval, laboratory assay availability, and clinical judgement.

**The optimal and maximum dosages of four factor prothrombin complex concentrate (4F-PCC) and factor eight inhibitor bypass activity (FEIBA) are not well defined; therefore, the dosing recommended within may be modified based on an individualized assessment of bleeding and thrombosis risk and institutional protocols.

Document allergies on approved form and ensure medication reconciliation has been reviewed as per organizational process

## Reversal & Hemostatic Therapies for DOAC-related, Life-Threatening Bleeding

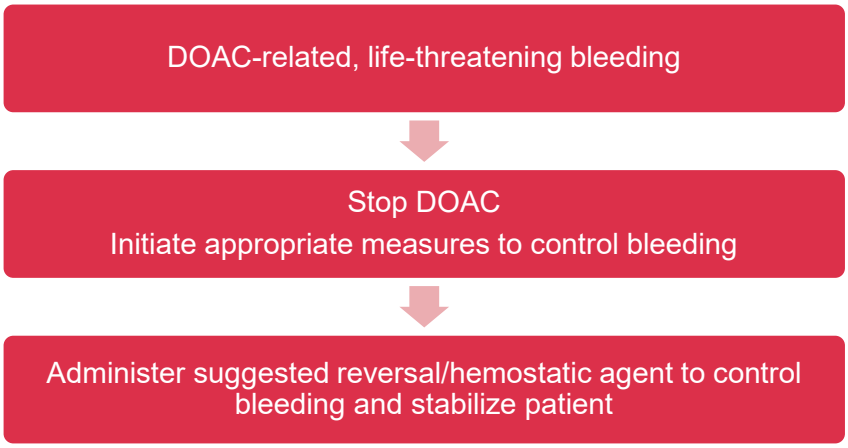
ACTION

## Administration

### DOCUMENT PURPOSE

This order set is intended for use in patients with life-threatening bleeding while receiving a direct-oral anticoagulant (DOAC) in whom clinically significant levels of DOAC are confirmed or suspected and for whom the decision to reverse anticoagulation has been made in addition to supportive measures. This order set is not intended for use for patients with mild bleeding or for emergent surgery/procedures.

### DECISION SUPPORT[1,2]:




## Lab Monitoring*

### ALL PATIENTS:

- ☐ Complete blood count (CBC)
- ☐ Metabolic panel including liver and kidney function
- ☐ Type and screen, crossmatch
- ☐ Prothrombin time/International Normalized Ratio (PT/INR)
- ☐ activated Partial Thromboplastin Time (aPTT)

***Do not delay administration of reversal agents for life-threatening bleeding while waiting for lab results***



Submitted by: _____ (ID) _____ (PRINTED NAME) _____ (YYYY-MM-DD HH:MM) ☐ Read Back

Practitioner: _____ (ID) _____ (PRINTED NAME) _____ (YYYY-MM-DD HH:MM) _____ (SIGNATURE)

Document allergies on approved form and ensure medication reconciliation has been reviewed as per organizational process

## Reversal & Hemostatic Therapies for DOAC-related, Life-Threatening Bleeding

ACTION

### DABIGATRAN PATIENTS:

- ☐ First-Choice: Dilute thrombin time (dTT), ecarin clotting time (ECT), or ecarin chromogenic assay (ECA) (if available)
- ☐ Second-Choice: Thrombin time (TT)

### APIXABAN, RIVAROXABAN, EDOXABAN PATIENTS:

- ☐ First-Choice: Anti-FXa chromogenic assay calibrated to specific DOAC (if available)
- ☐ Second-Choice: Anti-FXa assay calibrated to UFH or LMWH (if available)

## Medication*

**** Reversal agents are prioritized per guideline recommendations and should be used in the order listed, based on availability***

### APIXABAN (ELIQUIS®)[3]

☐ **ANDEXANET ALFA (ANDEXXA®)[4]**

**<8 HOURS OR UNKNOWN TIMING OF INGESTION:**

☐ Apixaban dose ≤5mg
- Andexanet alfa 400 mg IV bolus administered at rate of 30 mg/minute, followed within 2 minutes by continuous IV infusion of 4 mg/minute for up to 120 minutes

☐ Apixaban dose >5mg or unknown dose strength
- Andexanet alfa 800 mg IV bolus administered at a rate of 30 mg/minute, followed within 2 minutes by continuous IV infusion of 8mg/minute for up to 120 minutes

**≥8 HOURS SINCE INGESTION:**

☐ Andexanet alfa 400 mg IV bolus administered at rate of 30 mg/minute, followed within 2 minutes by continuous IV infusion of 4 mg/minute for up to 120 minutes



Submitted by: _____ (ID) _____ (PRINTED NAME) _____ (YYYY-MM-DD HH:MM) ☐ Read Back

Practitioner: _____ (ID) _____ (PRINTED NAME) _____ (YYYY-MM-DD HH:MM) _____ (SIGNATURE)

Document allergies on approved form and ensure medication reconciliation has been reviewed as per organizational process

| Reversal & Hemostatic Therapies for DOAC-related, Life-Threatening Bleeding | ACTION |
|---|---|

☐ **4 FACTOR PROTHROMBIN COMPLEX CONCENTRATE (4F-PCC) (KCENTRA®)[5]** (IF ANDEXANET ALFA IS UNAVAILABLE)**

- ☐ 2,000 units IV[2,3]
- ☐ 25-50 units/kg IV[2,3]

☐ **ACTIVATED CHARCOAL[2,3]**

**<2-4 HOURS SINCE INGESTION:**

- ☐ activated charcoal 50g orally

## DABIGATRAN (PRADAXA®)[6]

☐ **IDARUCIZUMAB (PRAXBIND®)[7]**

- ☐ Idarucizumab (Praxbind®) 5g IV (2.5g IV bolus x 2)

☐ **4 FACTOR PROTHROMBIN COMPLEX CONCENTRATE (4F-PCC) (KCENTRA®)[5] 50 UNITS/KG** OR ACTIVATED PCC (APCC) (FEIBA®)[8] 50 UNITS/KG** IV** (IF IDARUCIZUMB IS UNAVAILABLE)

☐ **ACTIVATED CHARCOAL[2,3]**

**<2-4 HOURS SINCE INGESTION:**

- ☐ activated charcoal 50g orally

☐ **NEPHROLOGY CONSULT FOR POSSIBLE HEMODIALYSIS[9]**

## EDOXABAN (SAVAYSA®)[10]

☐ **ANDEXANET ALFA (ANDEXXA®)[4]**

**REGARDLESS OF TIMING OF LAST DOSE:**

- ☐ Andexanet alfa 800 mg IV bolus administered at rate of 30 mg/minute, followed within 2 minutes by continuous IV infusion of 8 mg/minute for up to 120 minutes



Submitted by: _____ (ID) _____ (PRINTED NAME) _____ (YYYY-MM-DD HH:MM) ☐ Read Back

Practitioner: _____ (ID) _____ (PRINTED NAME) _____ (YYYY-MM-DD HH:MM) _____ (SIGNATURE)

## Reversal & Hemostatic Therapies for DOAC-related, Life-Threatening Bleeding

ACTION

☐ **4 FACTOR PROTHROMBIN COMPLEX CONCENTRATE (4F-PCC) (KCENTRA®)[5**] (IF ANDEXANET ALFA IS UNAVAILABLE)**

- ☐ 2,000 units IV[2,3]
- ☐ 25-50 units/kg IV[2,3]

☐ **ACTIVATED CHARCOAL[2,3]**

**<2-4 HOURS SINCE INGESTION:**

- ☐ activated charcoal 50g orally

### RIVAROXABAN (XARELTO®)[11]

☐ **ANDEXANET ALFA (ANDEXXA®)[4]**

**<8 HOURS OR UNKNOWN TIMING OF INGESTION:**

- ☐ Rivaroxaban dose ≤10 mg
  - Andexanet alfa 400 mg IV bolus administered at rate of 30 mg/minute, followed within 2 minutes by continuous IV infusion of 4 mg/minute for up to 120 minutes
- ☐ Rivaroxaban dose >10 mg or unknown dose strength
  - Andexanet alfa 800 mg IV bolus administered at a rate of 30 mg/minute, followed within 2 minutes by continuous IV infusion of 8 mg/minute for up to 120 minutes

**≥8 HOURS SINCE INGESTION:**

- ☐ Andexanet alfa 400 mg IV bolus administered at rate of 30 mg/minute, followed within 2 minutes by continuous IV infusion of 4 mg/minute for up to 120 minutes



Submitted by: _____ ID _____ PRINTED NAME _____ YYYY-MM-DD HH:MM ☐ Read Back

Practitioner: _____ ID _____ PRINTED NAME _____ YYYY-MM-DD HH:MM _____ SIGNATURE

Document allergies on approved form and ensure medication reconciliation has been reviewed as per organizational process

| Reversal & Hemostatic Therapies for DOAC-related, Life-Threatening Bleeding | ACTION |
|---|---|

☐ **4 FACTOR PROTHROMBIN COMPLEX CONCENTRATE (4F-PCC) (KCENTRA®)[5] ** (IF ANDEXANET ALFA IS UNAVAILABLE)**

- ☐ 2,000 units IV[2,3]
- ☐ 25-50 units/kg IV[2,3]

☐ **ACTIVATED CHARCOAL[2,3]**

**<2-4 HOURS SINCE INGESTION:**

- ☐ activated charcoal 50g orally



Submitted by: _____ ID _____ PRINTED NAME _____ YYYY-MM-DD HH:MM ☐ Read Back

Practitioner: _____ ID _____ PRINTED NAME _____ YYYY-MM-DD HH:MM _____ SIGNATURE

Document allergies on approved form and ensure medication reconciliation has been reviewed as per organizational process

## Reversal & Hemostatic Therapies for DOAC-related, Life-Threatening Bleeding

ACTION

### Additional Orders



Submitted by: _____ (ID) _____ (PRINTED NAME) _____ (YYYY-MM-DD HH:MM) ☐ Read Back

Practitioner: _____ (ID) _____ (PRINTED NAME) _____ (YYYY-MM-DD HH:MM) _____ (SIGNATURE)

## References

1. Tomaselli GF, Mahaffey KW, Cuker A, Dobesh PP, Doherty JU, Eikelboom JW, Florido R, Gluckman TJ, Hucker WJ, Mehran R, Messé SR, Perino AC, Rodriguez F, Sarode R, Siegal DM, Wiggins BS. 2020 ACC Expert Consensus Decision Pathway on Management of Bleeding in Patients on Oral Anticoagulants: A Report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol. 2020 Aug 4;76(5):594-622. doi: 10.1016/j.jacc.2020.04.053. Epub 2020 Jul 14. Erratum in: J Am Coll Cardiol. 2021 Jun 1;77(21):2760. PMID: 32680646.
2. Baugh CW, Levine M, Cornutt D, Wilson JW, Kwun R, Mahan CE, Pollack CV Jr, Marcolini EG, Milling TJ Jr, Peacock WF, Rosovsky RP, Wu F, Sarode R, Spyropoulos AC, Villines TC, Woods TD, McManus J, Williams J. Anticoagulant Reversal Strategies in the Emergency Department Setting: Recommendations of a Multidisciplinary Expert Panel. Ann Emerg Med. 2020 Oct;76(4):470-485. doi: 10.1016/j.annemergmed.2019.09.001. Epub 2019 Nov 13. PMID: 31732375; PMCID: PMC7393606.
3. Eliquis (apixaban) [prescribing information]. Princeton, NJ: Bristol-Myers Squibb Company; April 2021.
4. Andexxa (andexanet alfa) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; July 2022.
5. Kcentra (prothrombin complex concentrate [human]) [prescribing information]. Kankakee, IL: CSL Behring; October 2018.
6. Pradaxa (dabigatran etexilate) capsules [prescribing information]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals Inc; June 2021.
7. Praxbind (idarucizumab) [prescribing information]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals Inc: October 2021.
8. FEIBA (anti-inhibitor coagulant complex) [prescribing information]. Lexington, MA: Baxalta US Inc; February 2020.
9. Chai-Adisaksopha C, Hillis C, Lim W, Boonyawat K, Moffat K, Crowther M. Hemodialysis for the treatment of dabigatran-associated bleeding: a case report and systematic review. J Thromb Haemost. 2015 Oct;13(10):1790-8. doi: 10.1111/jth.13117. Epub 2015 Sep 29. PMID: 26270886.
10. Savaysa (edoxaban) [prescribing information]. Basking Ridge, NJ: Daiichi Sankyo Inc; April 2021.
11. Xarelto (rivaroxaban) [prescribing information]. Titusville, NJ: Janssen Pharmaceuticals Inc; January 2022



**Faculty:** Ronni Nemeth, PharmD, CACP, DPLA | Scott Kaatz, DO, MSc | Kyle DeWitt, PharmD, BCPS | Deb Siegal, MD, MSc, FRCPC

**This content was developed independently by the Anticoagulation Forum. Support for this project provided by AstraZeneca.**

Order Set Updated: January 2023



Submitted by: _____ ID _____ PRINTED NAME _____ YYYY-MM-DD HH:MM ☐ Read Back

Practitioner: _____ ID _____ PRINTED NAME _____ YYYY-MM-DD HH:MM _____ SIGNATURE