There is no pharmacologic antidote for factor Xa inhibitors, and treatment of bleeding remains empirical. Currently, limited evidence exists to guide clinicians in the management of factor Xa Inhibitor-associated bleeding events.

The following therapies for reversal have been tried, but outcomes do not support their use; and they are not recommended: antifibrinolytics (aminocaproic acid, tranexamic acid), recombinant factor VIIa (NovoSeven®), prothrombin complex concentrate (PCC—Profilnine®), and frozen fresh plasma.

### Minor Bleeding
(e.g., lacerations, post-dialysis bleeding, bleeding from a compressible site)
- Delay factor Xa inhibitor until there is adequate hemostasis
- Consider silver nitrate cauterization as applicable

### Major Bleeding
(e.g., active GI bleed, trauma, and uncontrollable epistaxis)
- Delay factor Xa Inhibitor until there is adequate hemostasis
- Oral activated charcoal if ingestion in last 2 hours (dose 1 g/kg of oral suspension – round to the nearest 25 grams)
- Fluid replacement and hemodynamic support
- Topical thrombin as appropriate
- If fibrinogen < 200 mg/dL, give 2 pools cryoprecipitate
- If platelets < 50 K/μL, give platelets
- Consider (in order of preference):
  1. 4-factor PCC (Kcentra®)*
  2. Anti-inhibitor coagulant complex (FEIBA®)*

### Life-Threatening Bleeding
(e.g., GI hemorrhage with hemodynamic compromise, retropharyngeal or retroperitoneal bleeding, intracranial hemorrhage, major trauma)
- Fluid replacement and hemodynamic support
- Topical thrombin as appropriate
- If fibrinogen < 200 mg/dL, give 2 pools cryoprecipitate
- If platelets < 50 K/μL, give platelets
- Consider (in order of preference):
  1. 4-factor PCC (Kcentra®)*
  2. Anti-inhibitor coagulant complex (FEIBA®)*

* Kcentra® and FEIBA® contain clotting factors and place patients at risk of thrombosis, including life-threatening arterial thrombosis.

** Please note there are limited data regarding the use of these agents to reverse factor Xa inhibitors.

** Consideration of the use of 4-factor PCC or anti-inhibitor coagulant complex may be undertaken, based on clinical judgment, for major uncontrolled bleeding if the bleeding is uncontrolled and the risk of clinical deterioration is high.

** In life-threatening bleeding, the benefit of 4-factor PCC or anti-inhibitor coagulant complex may outweigh the risk.

### Reversal Treatment

<table>
<thead>
<tr>
<th>Category</th>
<th>Medication</th>
<th>Factors</th>
<th>Dose**</th>
</tr>
</thead>
</table>
| 4-factor PCC                    | Kcentra®    | II, VII, IX, X, proteins C and S | - 25-50 units/kg  
  o Not to exceed 5000 units. 
  o Repeat dosing not recommended. |
| Anti-inhibitor coagulant complex, vapor treated | FEIBA® | II, VII, IX, X | - 25 units/kg  
  o If still clinically significant bleeding, consider re-dosing, but no sooner than 6 hours. |

**Doses are not well established for this indication
Baseline Labs

- Serum creatinine (chem-7)
- Ionized calcium (goal ionized: 4.6 – 5.3 mg/dL)
- CBC
- Prothrombin time (PT)
- Arterial or venous pH
  - During the process of resuscitation, attempt to achieve goal of pH > 7.25 to facilitate the effectiveness of reversal agents.
- Fibrinogen
  - Fibrinogen should not be reduced as a result of factor Xa inhibitor use but in the event it is low, steps to address it should be taken.

Monitoring

- Repeat ionized calcium, arterial or venous pH, CBC, fibrinogen, PT, 2 hours after each intervention
- Repeat at least every 6 hours x 24 hours and as indicated clinically.

<table>
<thead>
<tr>
<th>Lab Test</th>
<th>Normal Range (seconds)</th>
<th>Turnaround Time (minutes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PT</td>
<td>12.6 – 14.8</td>
<td>45 – 60</td>
</tr>
</tbody>
</table>

Consults

- Surgery consult as needed
- Consider Hematology consult for continued bleeding

References

- Rivaroxaban (Xarelto) Package Insert November 2011

Order Set

- OSU IP GEN: FACTOR XA ANTICOAGULANTS (RIVAROXaban, APIXaban) REVERSAL (3581)

Quality Measures

- Mortality rate
- Patient received necessary consults
  - Surgery
  - Hematology
- Percent of patients who received non-recommended therapies:
  - Antifibrinolytic therapy
  - Recombinant factor VIIa (NovoSeven®)
  - PCC (Profilnine®)
  - FFP
- Hospital length of stay (days)
- Rate of thrombosis in patients who received prothrombotic agent
  - Deep vein thrombosis (DVT)
  - Stroke
  - Pulmonary embolism (PE)
  - Myocardial infarction (MI)

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Guideline Approved


Disclaimer: Clinical practice guidelines and algorithms at The Ohio State University Wexner Medical Center (OSUWMC) are standards that are intended to provide general guidance to clinicians. Patient choice and clinician judgment must remain central to the selection of diagnostic tests and therapy. OSUWMC’s guidelines and algorithms are reviewed periodically for consistency with new evidence; however, new developments may not be represented.

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