Goal: Safe reversal of bleeding for patients taking Factor Xa Inhibitors.

Key Points:
- Order Set: OSU IP GEN: FACTOR XA ANTICOAGULANTS (RIVAROXABAN, APIXABAN) REVERSAL (3581)
- There is no pharmacologic antidote for factor Xa inhibitors, and treatment of bleeding remains empirical. Limited evidence exists to guide clinicians in the management of factor Xa Inhibitor-associated bleeding events.
- The following therapies for reversal factor Xa inhibitors have been tried, but outcomes do not support their use and they are not recommended:
  - Antifibrinolytics (aminocaproic acid, tranexamic acid)
  - Recombinant factor VIIa (NovoSeven®)
  - 3-factor prothrombin complex concentrate (PCC—Profilnine®)
  - Vitamin K
  - Frozen fresh plasma (FFP)

**Bleeding on Factor Xa Inhibitor — Emergent Reversal**

Obtain Baseline Labs – see page 2

- **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)
  - Stop factor Xa inhibitor until there is adequate hemostasis
  - Consider holding antiplatelet therapy
  - Oral activated charcoal if ingested 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/uL, 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, CNS hemorrhage, major trauma)
  - 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.

Follow up with proper monitoring – see page 2

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

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## Medication Factors

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

*Doses are not well established for this indication. Adjusted body weight should be used.

## Baseline Labs
- Serum creatinine (chem-6)
- CBC
- Prothrombin time (PT)
- Fibrinogen
  - If < 200 mg/dL, give 2 pools of cryoprecipitate

## Monitoring
- Repeat CBC, fibrinogen, PT, 2 hours after each intervention
- Repeat at least every 12 hours x 24 hours and as indicated clinically.

## Lab Test | Normal Range (seconds) | Turnaround Time (minutes)
--- | --- | ---
PT | 12.6 – 14.8 | 45 – 60

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

## References
- Rivaroxaban (Xarelto) Package Insert November 2011

## 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
  - Vitamin K
- Rate of thrombosis
  - 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.