Maine Medical Center
Guideline for the Management of Bleeding on
RIVAROXABAN (XARELTO®) or APIXABAN (ELIQUIS®)

Key Background

- Rivaroxaban and apixaban are direct factor Xa inhibitors. As such, replacing clotting factor(s) is not as effective in stopping bleeding as it is in settings with factor deficiency. There is currently no strong evidence that FFP, Factor VIIa, or Kcentra (4-factor prothrombin complex concentrate) can reduce the bleeding induced by rivaroxaban or apixaban. [R]
- Fresh frozen plasma will not reverse the anticoagulation effect of rivaroxaban or apixaban as the drug will inhibit factor Xa in the infused plasma. The prolonged clotting time with rivaroxaban and apixaban is a reflection of factor Xa inhibition rather than a clotting factor deficiency. [R]

General Care for All Patients

- Hold rivaroxaban/apixaban, [R]1,2
  - The half-life of rivaroxaban is 5-9 hours, but approaches 11-13 hours in the elderly. The half-life of apixaban is 8 hours for the 2.5 mg dose and 15 hours for the 5 mg dose. [R]
- Obtain laboratory studies including CBC, aPTT, INR*, CMP, fibrinogen activity, [C,R]3,4
- Evaluate for anatomic defects explaining hemorrhage, [R]1,2
- Use local measures to control bleeding, [R]1,2
- Consider the need for surgical intervention, embolization to control bleeding, [R]1,2
- Consider the need for Hematology consult. [R]1,2

*Typical therapeutic doses of rivaroxaban are associated with an INR <1.7. There is limited experience available for apixaban and laboratory testing. Anti-factor Xa assays have not been standardized to the new anticoagulants. [R]

For Patients with Mild Bleeding

- Continue “General Care for All Patients” listed above, and:
- Delay next rivaroxaban/ apixaban dose, [R]1,2
- Discontinue rivaroxaban/apixaban treatment if appropriate. [R]1
- Supportive care / symptomatic treatment. [R]1,2

For Patients with Moderate to Severe Bleeding

- Discontinue rivaroxaban/apixaban, [R]1,2
- Supportive care / symptomatic treatment, [R]1,2
- Activated charcoal at standard doses if last dose of rivaroxaban/apixaban within 1-2 hours, [R]7,10
- Maintain adequate diuresis with fluid replacement and hemodynamic support as needed, [B]1,7,8
- Transfuse RBCs as needed to maintain HgB above 8 gm/dL, [R]1,2
- If more than 4 units of RBCs are required, transfuse RBCs/plasma 1:1 to avoid a dilutional coagulopathy [B]
- See also Maine Medical Center Massive Transfusion Protocol

*Hemodialysis is not effective for the removal of rivaroxaban/apixaban due to high protein binding.

For Patients with Severe/Life Threatening Bleeding

- Continue “General Care,” and “Moderate to Severe Bleeding” measures above, and:
- Consider Kcentra (25 units/kg) to help with clot formation at the site of bleeding. [R]5
- As a last resort, consider recombinant activated Factor VII (20 mcg/kg) [R]1,7
- NOTE: The strength of the evidence for these interventions is weak and limited.

Grade R Evidence = Consensus Statement from Consensus Report or Narrative Review
Supporting Evidence


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Evidence Grading

Primary Reports of New Data Collections

A Randomized, controlled trial
B Cohort study
C Non-randomized trial with concurrent or historical controls
   Case-control study
   Study of sensitivity/specificity of a diagnostic test
   Population-based descriptive study
D Cross-sectional study
   Case series
   Case report

Reports that Synthesize or Reflect Upon Collections of Primary Reports

M Meta-analysis
   Systematic review
   Decision analysis
   Cost-effectiveness analysis
R Consensus statement
   Consensus report
   Narrative review
X Medical opinion