IREDELL HEALTH SYSTEM

Management of Bleeding Events with Direct Acting Oral Anticoagulants (DOAC)	
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Dabigatran (Pradaxa) – a direct thrombin inhibitor
The half-life varies with renal function: 12-17 hours for CrCl > 50 mL/min; 18 hours for CrCl 30-50 mL/min; and 28 hours for CrCl < 30 mL/min.

Idarucizumab (Praxbind) is an immediate and specific reversal agent for Pradaxa. It is indicated when reversal is needed in patients who are at least 18 years of age with one of the following criteria: (1) life-threatening or uncontrolled bleeding; or (2) need for emergency surgery/urgent procedures that cannot be delayed for at least 8 hours, where normal hemostasis is required and patient received dose of Pradaxa within the last 48 hours.

Praxbind is not intended for use for:

1) minor or nuisance bleeding/bruising in clinically stable individuals;
2) patients for whom simple support, monitoring, or time prior to a surgical procedure is appropriate;
3) elective procedures or surgeries.

- aPTT elevation is consistent with ingestion, but it does not correlate with the degree of anticoagulation. If aPTT is normal, dabigatran is likely not the etiology of the bleeding.
- Activated charcoal is an option for decreasing absorption if given within 2 hours of ingestion of Pradaxa.
- Adequate diuresis is necessary for excretion, since Pradaxa is primarily renally eliminated.
- Hemodialysis is effective in removing up to 65% of Pradaxa.
- Protamine sulfate and vitamin K are not expected to affect the anticoagulant activity of Pradaxa.
- Use of FFP for bleeding management with Pradaxa has not been evaluated in clinical studies.

Bleeding Severity	Management Recommendations for Pradaxa
Mild	Delay next dose or discontinue Pradaxa. Reversal agent is not indicated.
Moderate To Severe	Discontinue Pradaxa. Consider any of the following based on bleeding severity and location: • Symptomatic treatment • Mechanical compression • Surgical intervention • Fluid replacement and hemodynamic support • Adequate diuresis for Pradaxa elimination (consider IVF, diuretics) • Blood product transfusion • Oral activated charcoal (if last Pradaxa dose ingested within 2 hours) Dose: liquid charcoal with sorbitol 50 grams po/per tube x 1 dose

	• Administration of platelet concentrates in cases where significant thrombocytopenia is present or long-acting antiplatelet drugs have been used • To investigate potential causes of bleeding, obtain the following STAT labs: CBC, PT, aPTT, serum creatinine, type and screen.
Life-threatening OR Uncontrolled bleeding OR Need for emergency surgery/urgent procedure (within the next 8 hours)	Discontinue Pradaxa. *Consider any of the strategies outlined above based on bleeding severity* • Praxbind (idarucizumab) 5 grams IV. If clinically relevant bleeding along with elevated coagulation parameters reappears, or if patient requires a second emergency surgery/urgent procedure and has elevated coagulation parameters, an additional full dose may be considered. • Blood products if needed for hemodynamic support: For FFP, efficacy is unknown and large volumes may be needed.

Factor Xa inhibitors – rivaroxaban (Xarelto), apixaban (Eliquis) , edoxaban (Savaysa), betrixaban (Bevyxxa)
The half-life varies between agents and is dependent upon renal function. Renal Excretion ranges from approximately 11 to 35 percent amongst all the factor Xa inhibitors.

- Activated charcoal is an option for decreasing absorption if given within 2 hours of ingestion of factor Xa inhibitors.
- Protamine sulfate and vitamin K are not expected to affect the anticoagulant activity of factor Xa inhibitors.
- Factor Xa inhibitors are not expected to be dialyzable, because they are highly protein-bound.

Use of Fresh Frozen Plasma (FFP) to reverse the anticoagulant effect of Factor Xa Inhibitors has not been evaluated in clinical studies.

Use of procoagulant reversal agents such as prothrombin complex concentrates, recombinant Factor VIIa (Novoseven), and activated prothrombin complex concentrate (such as K-Centra) may be considered for life-threatening bleeding; none have been definitively demonstrated to work in the setting of DOAC-associated bleeding. These agents are associated with thrombotic complications, so the risk of bleeding versus the risk of thrombosis must be considered. These agents should not be used if the patient has experienced a thrombotic or thromboembolic event in the past 6 weeks (such as DVT, PE, ischemic stroke, traumatic injury, ACS, acute mesenteric ischemia, acute peripheral - arterial ischemia).

Andexanet alfa (Andexxa) is a reversal agent for factor Xa inhibitors. It was approved by the FDA in May of 2018 for the reversal of anticoagulation by rivaroxaban and apixaban in individuals with life-threatening or uncontrolled bleeding associated with these agents. *Andexanet alfa (Andexxa) is not a formulary item at Iredell Health System.* 4-Factor PCC is a reasonable alternative; these agents have not been compared directly in a randomized trial. Therefore, the interventions below may be considered but are not required in the management of bleeding associated with the use of these agents.

Bleeding Severity	Management Recommendations Factor Xa Inhibitors
Mild	Delay next dose or discontinue Factor Xa Inhibitor.
Moderate to Severe	Discontinue Factor Xa Inhibitor. Consider any of the following based on bleeding severity and location: • Symptomatic treatment

	• Mechanical compression • Surgical intervention • Fluid replacement and hemodynamic support • Blood product transfusion • Oral activated charcoal, if last Factor Xa Inhibitor dose ingested recent enough (rivaroxaban within 8 hours, apixaban within 6 hours, edoxaban within 2 hours) • Dose: liquid charcoal with sorbitol 50 grams PO/per tube x 1 dose • Administration of platelet concentrates in cases where significant thrombocytopenia is present or long-acting antiplatelet drugs have been used. • To investigate potential causes of bleeding, obtain the following STAT labs: CBC, PT, aPTT, serum creatinine, type and screen. *If hemostasis is not achieved with the strategies outlined above, consider proceeding to the steps below.*
Life-threatening or Intracranial hemorrhage	*Consider any of the strategies outlined above based on bleeding severity:* **If intracranial hemorrhage (ICH) or CNS process:** K-Centra (4-factor PCC) 50 units/kg IV STAT x 1 dose. Pharmacy to round to the nearest vial using actual body weight (maximum dose = 5,000 units). **If extracranial or non-CNS process:** K-Centra (4-factor PCC) 2,000 units IV STAT x 1 dose. (If body weight <40 kg, only administer 50 units/kg x1. • May repeat K-Centra (4-factor PCC) 1000 units IV x1 if inadequate response to initial dose in 1 – 2 hours. If PT is prolonged, consider administering vitamin K 10 mg IV x 1 dose over 30 minutes (as there may be vitamin K deficiency present).

The content of this policy and procedure serves as guidance to the delivery of quality patient care. Care providers are expected to exercise critical thinking and situational awareness skills and in specific situations to take such action as is necessary for the delivery of quality patient care.

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