

Anticoagulation Therapy: Use of Dabigatran and Rivaroxaban

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Contributors to this issue:

Updates in Anticoagulation: Dabigatran and Rivaroxaban
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Cautions and Clinical Pearls:

-dabigatran capsules should NOT be broken, chewed or opened before administration

-severe hepatic dysfunction may impair metabolism of rivaroxaban, although no dose adjustment recommendations

-monitor renal function in patients with nonvalvular atrial fibrillation treated with dabigatran or rivaroxaban

Dosing:

URMC adult dabigatran guideline available on Pharmacy Sharepoint site
Rivaroxaban guideline available soon

Orthopedic surgery:

Rivaroxaban offers the clinician once daily dosing for postoperative DVT prophylaxis in patients who undergo knee or hip surgery with no laboratory monitoring necessary

How Supplied:

Xarelto® (rivaroxaban) 10 mg, 15 mg, 20 mg tablets

Pradaxa® (dabigatran) 75 mg and 150 mg capsules

In the world of oral anticoagulation therapy, warfarin has been the lone contender for over 50 years. Two new agents, allowing alternatives over traditional warfarin therapy, have recently been approved by the FDA and more are in the works. Dabigatran (Pradaxa®) was approved in 2010 for stroke prevention in nonvalvular atrial fibrillation. Rivaroxaban (Xarelto®) was approved in 2011 for both thromboprophylaxis after orthopedic surgery and stroke prevention in nonvalvular atrial fibrillation. This article discusses important points of anticoagulation therapy using these new thrombotic agents.

What is the mechanism of action?

Both agents inhibit specific areas of the coagulation cascade, thereby inhibiting thrombus formation.

- dabigatran is a direct thrombin inhibitor
- rivaroxaban is a direct factor Xa inhibitor

What are the benefits over warfarin?

- no laboratory monitoring required
- less number of drug-drug and food interactions
- fixed dosing with renal adjustment recommendations
- once daily dosing for rivaroxaban
- rapid onset
 - 1 to 2 hours with dabigatran
 - 2 to 4 hours with rivaroxaban

Who is a good candidate for therapy?

- nonvalvular atrial fibrillation with an indication for oral anticoagulation (CHADS₂ score of ≥ 1)
- warfarin naïve or difficult to control with warfarin
- laboratory monitoring compliance issues
- good medication compliance
- little to no renal dysfunction
- no history of major bleeding events while on anticoagulation therapy

*Patients already on a stable regimen should NOT be switched to an alternative agent

How do I switch patient from or to warfarin therapy?

-dabigatran: URMC has published guidelines with specific conversion tables when transitioning from or to warfarin, as well as recommendations for discontinuation for surgical procedures.

Guidelines are available on the anticoagulation site on the SMH Pharmacy Sharepoint page. Follow this link: <http://inside.mc.rochester.edu/sites/Pharmacy/default.aspx>

-rivaroxaban: URMC guidelines to be published soon.

Is there a method to determine whether a patient is anticoagulated on these agents?

-no specific laboratory test to determine how well patient is anticoagulated

Many labs may be elevated, i.e. aPTT, TT, and INR, although NO therapeutic range has been identified. An elevated aPTT is a good marker for drug compliance with dabigatran and possibly with rivaroxaban.

***Self-awareness of bleeding risk is a very important counseling point due to lack of monitoring and parameters for determining anticoagulation. Remind patients to report all instances of trauma and bleeding.**

What can be done to reverse an acute overdose or bleeding event due to these agents?

- no approved reversal agents for either dabigatran or rivaroxaban
- hemodialysis is the only option for reversal of bleeding from dabigatran, but there are obvious drawbacks to initiating that procedure in a patient who is bleeding
- *rivaroxaban is NOT thought to be dialyzable probably because of the high protein binding of the drug
- four factor prothrombin complex concentrates may be useful for both dabigatran and rivaroxaban but more studies need to be done
- URMC will publish guidance in the near future

Editors note:

*Dr. Spyropoulos is one of the authors of an article titled, *Guidance on the emergent reversal of oral thrombin and factor Xa inhibitors*, Am J Hematol, 2012 Mar14
Link: <http://tq7xh3ee6l.search.serialsolutions.com/find?sid=Entrez:PubMed&id=pmid:22473649>

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