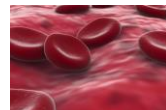


# CLOT



## Is Dabigatran (Pradaxa®) an Option for Your Patient?

### Indications<sup>1</sup>

- Non-Valvular Atrial Fibrillation (NVAf)\* to prevent stroke & systemic embolism
- Acute VTE treatment & prevention of recurrent VTE [for deep vein thrombosis (DVT) and pulmonary embolism (PE)]
- Prevention of venous thromboembolic events (VTE) in elective total hip or knee replacement surgery (THR, TKR)

\*CCS definition: AF without mechanical heart valves, rheumatic mitral stenosis, or moderate/severe non-rheumatic mitral stenosis<sup>2</sup>

### Requirements<sup>1</sup> - NOTE: Dabigatran accumulates in renal dysfunction.

- Stable creatinine clearance (CrCl) 30 mL/min or more

### Contraindications<sup>1,2</sup>

- Mechanical heart valves<sup>1,3</sup>
- Dabigatran, like other anticoagulants, is contraindicated in patients at high risk for bleeding
- Pregnant/Breastfeeding: Safety & dosing has not been studied. Use is NOT recommended
- Drug Interactions: Significant drug interactions involving P-glycoprotein - See below.

### Potential Limitations<sup>1</sup>

- Not recommended in hemodynamically unstable acute PE or those requiring thrombectomy or thrombolysis
- Drug Interactions: AVOID rifampin, select azole antifungals & anticonvulsants, HIV protease inhibitors, ticagrelor, St. John's Wort, and other strong P-gp inducers and inhibitors as there is minimal knowledge of clinical outcomes
- Combination therapy with antiplatelets increases bleeding risk
- Rapid decline in anticoagulant effect after a missed dose; adherence is critical
- Very limited data with extremes of weight (under 50 kg; over 120 kg or BMI > 40)<sup>4</sup>
- Less than 18 years of age: Safety and dosing has not been established
- Acute treatment of VTE: Must be preceded by 5-10 days of parenteral anticoagulant
- Dyspepsia
- AF: dabigatran 150mg BID showed higher GI bleed rate than warfarin, but no difference in overall bleeding events<sup>5</sup>

### May offer an advantage over warfarin if:

- Difficulty stabilizing on warfarin for reasons other than poor medication adherence
- INR monitoring is problematic (e.g. poor venous access, frequent travel, remote location). NOTE: Use of warfarin with point-of-care (POC) INR testing (e.g. CoaguChek XS™) may be an alternative solution
- AF: superior reduction in rate of stroke and systemic embolism with dabigatran 150 mg bid, lower rate major bleeding with 110 mg bid, lower intracranial hemorrhage with both doses vs. warfarin<sup>5</sup>
- Availability of idarucizumab for emergency surgery/urgent procedures or life-threatening/uncontrolled bleeding.<sup>6,7</sup>

### Dosing Recommendations<sup>1</sup>

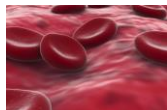
Indication	CrCl 50 mL/min or greater	CrCl 30–49 mL/min	CrCl less than 30mL/min
Stroke Prevention in Non-Valvular Atrial Fibrillation	<ul style="list-style-type: none"> <li>• 150 mg BID</li> <li>• 110 mg BID if ≥ 80 years of age. Also consider if &gt;75 years old <u>and</u> ONE or more risk factor for bleeding (e.g. CrCl 30 - 49 mL/min, on antiplatelets, or interacting medication, etc.)</li> </ul>		Contraindicated
Acute DVT/PE Treatment	Parenteral Anticoagulant x 5-10 days, then dabigatran as per AF dosing <sup>#</sup>		
Hip & Knee Replacement	110 mg initial dose*, then 220 mg once daily x 10 (TKR) to 28-35 days (THR)	75 mg initial dose*, then 150 mg once daily x 10 (TKR) to 28-35 days (THR)	

<sup>#</sup> 110 mg BID dose not studied for VTE treatment, but is suggested as per AF indication above<sup>1</sup>

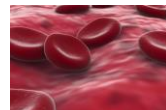
\*Initiate 1-4 h after surgery once hemostasis secured. If not started day of surgery, initiate with 220 mg once daily

### Inform Your Patient:

- Atrial Fibrillation: Should decrease risk of stroke by at least 2/3, compared to no anticoagulation
- Carry information indicating they are on an anticoagulant and inform their healthcare providers, including dentists
- Product monograph indicates must remain in original blister package or manufacturer's bottle.<sup>1</sup> Recent data indicates stability outside of the manufacturer's blister packs, but the clinical implications of this storage are not yet known<sup>8</sup>
- Swallow capsule whole - no chewing, crushing, or opening capsule as this may dramatically ↑ blood drug levels
- Must be taken TWICE daily with or without food; adherence is essential to avoid treatment failure
- Report symptoms/signs of dyspepsia bleeding, stroke, DVT/PE
- Cost varies by drug plan coverage and/or provincial criteria



# CLOT



## Monitoring Patients on Dabigatran

- CrCl should be determined at baseline and at least annually. Monitor more frequently if older than 75y, with renal dysfunction (CrCl <60 mL/min), or when a decline in renal function suspected
- Monitor for symptoms and signs of bleeding
- No routine coagulation testing required. NOTE: INR is not useful for monitoring. Do not target INR 2 to 3.
- If excess anticoagulation suspected, or to determine presence of dabigatran, an aPTT or more specifically a Thrombin Time (TT) may be considered. Normal values indicate little to no dabigatran present; however, a normal aPTT does not exclude presence of residual dabigatran. Specialized testing (e.g. dilute TT, Hemoclot™) may not be widely available, and should only occur in consultation with an expert in anticoagulation.

## Switching Between Agents<sup>1</sup>

### **From warfarin to dabigatran:**

- Discontinue warfarin and start dabigatran once INR is less than 2

### **From non-warfarin anticoagulant (oral or parenteral - e.g. LMWH, rivaroxaban, apixaban, edoxaban) to dabigatran:**

- Start dabigatran 0 - 2 hours before the next scheduled dose of non-warfarin anticoagulant was to be administered
- For agents administered by continuous infusion, stop the infusion and start dabigatran at the same time

### **From dabigatran to warfarin:**

- Start warfarin and only discontinue dabigatran once INR is 2 or greater

### **From dabigatran to non-warfarin anticoagulants (oral or parenteral): (e.g. LMWH, rivaroxaban, apixaban, edoxaban)**

- CrCl 30 mL/min or greater: Give 1<sup>st</sup> dose of non-warfarin anticoagulant 12 hours after the last dose of dabigatran
- CrCl Less than 30 mL/min: Give 1<sup>st</sup> dose of non-warfarin anticoagulant 24 hours after the last dose of dabigatran<sup>9</sup>

## Management of Bleeding Episodes with Dabigatran

- Idarucizumab (Praxbind™) is a rapid acting, target specific antidote, administered as an IV infusion / IV bolus for life threatening/uncontrolled bleeding or for emergency surgery/urgent procedures<sup>7</sup>
- Vitamin K, protamine and/or plasma will not reverse drug effects
- In the event of major hemorrhagic complications, discontinue dabigatran and refer patient for urgent assessment and locally developed management strategies
- PCC/activated PCC may reverse anticoagulant effect<sup>10</sup>, but the effect of these agents on bleeding outcomes is limited

## Anticoagulation around Invasive Procedures<sup>11</sup> (e.g. surgery, elective day procedures, major dental procedures)

- As with warfarin, very low risk bleed procedures (such as dental extraction) do not require withholding dabigatran
- Management plans should be made in consultation with the provider performing the procedure
- Renal function significantly impacts clearance of dabigatran. If the recommendations below cannot be met, consultation with an expert in anticoagulation management is encouraged.
- Due to the onset/offset time of dabigatran, peri-procedural use of LMWH is not required

### Pre-Procedure- If required, stop dabigatran before procedure as follows:

Renal function# (CrCl mL/min)	Last intake of drug prior to procedure	
	Low Bleeding Risk	High Bleeding Risk*
80 or more	at least 24 hours	at least 48 hours
50 - 79	at least 36 hours	at least 72 hours
30 - 49	at least 48 hours	at least 96 hours

# If CrCl less than 30 mL/min, dabigatran is contraindicated: Hold drug at least 5 days<sup>1</sup>

\* Make a careful decision (i.e. hold longer) for patients undergoing major surgery, spinal puncture, or other regional anaesthesia in whom complete hemostasis is required. Consult specialist in these high risk patients/procedures.

For an interactive perioperative management algorithm, see Thrombosis Canada website:

[http://thrombosiscanada.ca/?page\\_id=502&calc=perioperativeAnticoagulantAlgorithm](http://thrombosiscanada.ca/?page_id=502&calc=perioperativeAnticoagulantAlgorithm)

**Post Procedure:** Resumption should not be initiated until adequate hemostasis has been achieved and clinical situation allows (usually 1 -3 days). NOTE: Full therapeutic effect occurs approximately 2 hours after ingestion.

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11. Steffel J, et al. Eur Heart J 2018; 39:1 330-1393.