

Pradox[®] (*Dabigatran Etexilate*)

Anticoagulant/Thrombin Inhibitor¹

Available Products/Cost²: 75mg strength (30 caps) ~\$126
110mg strength (30 caps) ~\$126

Mechanism of Action¹

Dabigatran etexilate is a prodrug, which is converted to the active drug, dabigatran. Once activated, it's a competitive, reversible, direct thrombin inhibitor, which inhibits both free and fibrin-bound thrombin as well as thrombin-induced platelet aggregation.

Indications³

- *Labeled use* - Postoperative thromboprophylaxis in patients who have undergone total hip or knee replacement procedures
- *Unlabeled use* - Prevention of stroke and systemic embolism in patients with nonvalvular atrial fibrillation.

Dosing / Administration¹

	Initial	Maintenance
Adults	110mg 1-4 hours after surgery completion & establishment of hemostasis	220mg once daily
	220 mg once daily (if started any day other than the day of surgery)	
Special Patient Populations (a) >75 years old, (b) Moderate renal impairment (30-50mL/min), OR (c) Patient taking amiodarone	75mg 1-4 hours after surgery	150 mg once daily

Therapy Duration¹: Knee: 10 days

Hip: 28-35 days

Administration Requirements: Take with water and without regard to meals.¹

Storage: Discard 30 days after opening bottle.¹

Adverse Effects¹

- Bleeding (8-14%; major <2%)
- GI hemorrhage (<1%)
- Anemia (1-4%)
- Hematoma (1-2%)
- Hemoglobin decreased (1-2%)
- Hemorrhage (postprocedural or wound: 1-2%)
- ALT increased (>x ULN: 2-3%)
- Hematuria (1%)

Contraindications¹

- Hypersensitivity to the active substance or to any of the excipients
- Severe renal impairment ($Cl_{cr} < 30$ mL/min)
- Active clinically significant bleeding
- Organic lesion at risk of bleeding
- Spontaneous or pharmacological impairment of haemostasis
- Hepatic impairment or liver disease expected to have any impact on survival
- Concomitant treatment with quinidine

Warnings/Precautions¹

- Patients with conditions such as severe uncontrolled hypertension, congenital or acquired bleeding disorders, thrombocytopenia, renal impairment or recent major bleeding are at an increased risk of bleeding and should be monitored for signs and symptoms of a bleed.

- Avoid use in patients undergoing anesthesia with postoperative indwelling epidural catheters.
- Avoid use in patients with elevated hepatic transaminases >2 times ULN.

Drug Interactions³

Avoid concomitant use with: P-glycoprotein inhibitors & Quinidine

Dabigatran may increase effect/toxicity of: Anticoagulants, Ibritumomab, Tositumomab, and Iodine I 131 Tositumomab.

Levels/effects of Dabigatran may be increased by: Amiodarone, Antiplatelet agents, Dasatinib, Herbs (Anticoagulant/antiplatelet properties), Metronidazole systemic, NSAIDS, Pentosan Polysulfate Sodium, P-gp Inhibitors, Prostacyclin Analogues, Quinidine, Salicylates, thrombolytic agents

Levels/effects of Dabigatran may be decreased by: Antacids, Atorvastatin, P-gp inducers, Proton Pump Inhibitors, St John's wort

Pregnancy & Lactation⁴: Not studied; only take if benefit outweighs the risk.

Children⁴: Safety and effectiveness not established.

Pharmacokinetics¹

Bioavailability: ~ 6.5%

Half-Life: 11 hours (elderly 14-17 hours)

Advantages of Dabigatran⁵

- Oral administration
- Once daily dosing
- Minimal dose adjustments
- No INR monitoring
- Immediate onset of anticoagulation

Efficacy⁵

Three large phase III trials have been conducted to evaluate safety/efficacy of dabigatran versus enoxaparin for VTE prophylaxis following hip or knee surgery. Dabigatran appears as safe and effective as enoxaparin 40mg once daily (European dose) for VTE prevention. However, one study comparing dabigatran to Enoxaparin 30mg twice daily (Canadian dose) found dabigatran less effective.

Safety⁵

Bleeding rates are similar between dabigatran and enoxaparin in the major trials comparing these agents. Dabigatran was otherwise well tolerated.

Drug Status⁵

Dabigatran is approved for use in Canada but the Common Drug Review has recommended against listing dabigatran in formularies.

References

1. Pradox (dabigatran etexilate) [product monograph]. Burlington, ON. Boehringer Ingelheim Canada 2009.
2. McKesson Canada. PharmaClik: Pradox. Saint-Laurent, QB; c2005. Accessed March 15, 2010. <<http://clients.mckesson.ca>>
3. Lexi-Drugs (iPharmacist). Dabigatran Etexilate. Accessed March 9, 2010.
4. Lexi-Comp Inc. Dabigatran Etexilate. Ohio. Accessed March 15, 2010. <<http://online.lexi.com.cyber.usask.ca/crlsql/servlet/crlonline?siteid=293>>.
5. Saskatchewan Drug Information Services. New Oral Anticoagulants. 27(1). February 2010. <www.druginfo.usask.ca/pdf/New_Oral_Anticoagulants.pdf>