STEPS
New Drug Reviews

Dabigatran (Pradaxa) for Prevention of Stroke in Atrial Fibrillation

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STEPS new drug reviews cover Safety, Tolerability, Effectiveness, Price, and Simplicity. Each independent review is provided by authors who have no financial association with the drug manufacturer.

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Dabigatran (Pradaxa) is an orally administered direct thrombin inhibitor labeled for the prevention of stroke and systemic embolism in patients with nonvalvular atrial fibrillation. Unlike warfarin (Coumadin), it does not induce anticoagulation through depletion of clotting factors, but through an immediate effect on thrombin, the last step in the coagulation cascade that causes clot formation.

Drug	*Dosage*	*Dose form*	*Cost of full course**
Dabigatran (Pradaxa)	150 mg twice daily; 75 mg twice daily in patients with impaired renal function	75- and 150-mg capsules	$246 for 60 150-mg capsules

**—Estimated retail price of one month's treatment based on information obtained at http://www.drugstore.com (accessed October 25, 2010).*

SAFETY

Dabigatran increases the risk of minor and major bleeding. In a randomized controlled trial of dabigatran compared with dose-adjusted warfarin (International Normalized Ratio of 2.0 to 3.0) in more than 18,000 patients with atrial fibrillation, life-threatening bleeding and intracranial hemorrhage occurred less often with dabigatran, with one fewer patient experiencing an intracranial hemorrhage for every 117 patients treated with dabigatran instead of warfarin (number needed to treat [NNT] = 117; 95% confidence interval [CI], 82 to 201).[1] Although gastrointestinal bleeding occurs more often with dabigatran, the incidence of minor bleeding is lower (NNT = 37; 95% CI, 23 to 99).[1] Unlike warfarin, dabigatran lacks significant drug interactions. However, the concurrent use of antiplatelet agents, heparin, or long-term nonsteroidal anti-inflammatory drugs may increase the risk of bleeding. There is no reversal agent for dabigatran. It is renally eliminated, and the dosage must be reduced in patients with a creatinine clearance of less than 30 mL per minute per 1.73 m^2 (0.50 mL per second per m^2).[2] Dabigatran has not been studied in children or in pregnant or breastfeeding women. It is a U.S Food and Drug Administration pregnancy category C drug.

TOLERABILITY

In clinical trials, more patients receiving dabigatran withdrew because of adverse effects compared with those receiving warfarin. Dabigatran causes dyspepsia and gastritis symptoms in about one-third of patients.[2]

EFFECTIVENESS

Dabigatran has been compared with enoxaparin (Lovenox) and warfarin in randomized controlled trials. In a study of 18,000 patients with atrial fibrillation, those who received dabigatran had significantly fewer ischemic strokes than those who received warfarin for a median of two years (NNT = 91; 95% CI, 59 to 194).[1] Dabigatran has been studied for surgery prophylaxis (versus enoxaparin) and for the treatment of deep venous thrombosis

and pulmonary embolism (versus warfarin), but it is not labeled for these uses.[3-5]

PRICE

A one-month supply of 150-mg dabigatran capsules costs approximately $246; a one-month supply of generic warfarin costs approximately $15.[6] The lack of laboratory monitoring or office visits for dose titration may partially offset this difference.

SIMPLICITY

Dabigatran produces an effect on coagulation in 30 to 90 minutes, has a predictable response, does not require routine laboratory monitoring, and does not have the drug and food interactions that can be problematic with warfarin therapy. Patient compliance with twice-daily dosing must be stressed. The dose of dabigatran is fixed and does not require titration when therapy is initiated or discontinued.

Bottom Line

Dabigatran is superior to warfarin for stroke prevention in patients with atrial fibrillation, with similar rates of major bleeding. Because it does not require laboratory monitoring, dabigatran therapy is less complicated than warfarin therapy, but it costs significantly more.

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