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the maryland poison center's monthly update. news. advances. information.
1-800-222-1222
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Dabigatran (Pradaxa®)

Dabigatran (Pradaxa®) is an oral anticoagulant that is a reversible direct inhibitor of thrombin. It is indicated for the prophylaxis of venous thromboembolism in patients with atrial fibrillation. Dabigatran is renally excreted with a half-life of 12–17 hours. It is not metabolized by the CYP P450 system and does not inhibit or induce CYP 450 enzymes; therefore, it has a better drug interaction profile than other anticoagulants such as warfarin. The primary adverse effect with dabigatran is bleeding, including intracerebral hemorrhage.

When assessment of anticoagulation is necessary, the international normalized ratio (INR) is ineffective due to its lack of sensitivity (*Thromb Haemost 2010;103(6):1116–1127)*. Although activated partial thromboplastin time (aPTT) and thrombin clotting time (TT) lack sensitivity at high dabigatran concentrations, they may be used as a qualitative test to determine the presence of anticoagulant effect. Ecarin clotting time (ECT) is an assay for thrombin generation. It can be used, if available, as a quantitative test since there is a linear relationship between dabigatran blood levels and ECT. Additionally, ECT is not altered by the presence of concomitant anticoagulants.

Little information on acute overdoses exists; however, bleeding would be expected. Dabigatran therapy should be withheld and activated charcoal administered shortly after acute overdoses to prevent absorption. In instances of renal impairment or severe acute overdoses, the clearance of dabigatran may be increased by hemodialysis. In one study, more than 60% of a single dose was removed with 2-4 hours of hemodialysis *(Clin Pharmacokinet 2010;49:259–268)*. Dabigatran is not a vitamin K antagonist, therefore, vitamin K will not reverse its effects. Supportive measures such as mechanical compression, surgical intervention, or transfusion of blood products can be used to try to stop or minimize bleeding. Last line interventions to control bleeding include recombinant activated factor VII as well as prothrombin complex concentrates. Activated factor VII reverses other direct thrombin inhibitors, albeit inconsistently. Prothrombin complex concentrates have been found to help reverse or reduce the anticoagulation effect of dabigatran in animal studies.

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DID YOU KNOW THAT… *the FDA is reviewing reports of serious bleeding with Pradaxa® (dabigatran)?*

A clinical trial of 18,000 patients comparing Pradaxa® with warfarin showed that the rate of major bleeding events was similar for both drugs. The FDA released a safety communication on December 7, 2011 stating that it is evaluating post-marketing reports of bleeding with Pradaxa® to determine whether the actual frequency of events is as expected and if there is evidence of inappropriate dosing, drug interactions or other factors that might lead to bleeding. Additional information for healthcare professionals and patients is at http://www.fda.gov/Drugs/DrugSafety/ucm282724.htm .

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