Pradaxa® and warfarin have same risk of bleeding

On November 2, 2012 the FDA released a new Drug Safety Communication regarding the risk of bleeding with use of Pradaxa® (dabigatran). A safety review indicates that the risk of bleeding when initiating dabigatran therapy is similar to the risk of bleeding when initiating warfarin therapy.

This announcement is an update to a FDA Drug Safety Communication released on December 7, 2011 that reported a large number of serious bleeding events with dabigatran, after which the FDA began investigating whether the incidence of these events were higher than originally reported in clinical trials. This updated safety announcement supports the original claim from the RE-LY trial. Results of the trial suggested the rates of major hemorrhage between dabigatran 150mg twice daily and warfarin were similar.

To compare the rates of bleeding, the FDA looked at rates of gastrointestinal bleeds and intracranial hemorrhage through health insurance claims and administrative data available through the Mini-Sentinel project, a part of the FDA's Sentinel Initiative. This was done in efforts to get a clearer picture of the bleeding risk, as the previous announcement was based on reports to the Adverse Events Reporting System (AERS) database. The AERS database would inherently show bias toward warfarin, since the bleeding risk of warfarin is well established and not likely to be frequently reported by health care professionals. Data from the analysis show that risk of intracranial and gastrointestinal hemorrhage is 2.1-3.0 times and 1.6-2.2 times higher in new users of warfarin than new users of dabigatran, respectively. The consensus is that bleeding rates are not higher with new dabigatran use than with new warfarin use.

Pradaxa®'s package insert recommends reducing the dose of dabigatran if the patient's creatinine clearance is 15-30ml/hr and does not provide dose recommendations for creatinine clearance <15ml/hr. Signs and symptoms of major bleeding include unusual bruising, pink or brown urine, red or black tarry stools, coughing up blood, vomiting blood or vomit that looks like coffee grounds, pain, swelling or discomfort in a joint, headaches, dizziness, weakness, reoccurring nose bleeds, unusual bleeding from gums, bleeding that takes a long time to stop, menstrual or vaginal bleeding that is heavier than normal, dyspepsia, burning or nausea, abdominal pain or discomfort, or indigestion.

References

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- Connolly SJ, the RE-LY Steering Committee and Investigators, et al. Dabigatran versus Warfarin in Patients with Atrial Fibrillation. The New England Journal of Medicine. Sep 17, 2009. 361(12):1139-51.

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