

23 July 2014

Efficacy and Safety Profile of Pradaxa® (dabigatran etexilate) Repeatedly Confirmed

British Medical Journal issues unbalanced article regarding Pradaxa®

[For media outside UK, U.S. and Canada](#)

Ingelheim, Germany, July 23, 2014 – Boehringer Ingelheim wants to set the record straight following misleading statements that the British Medical Journal (BMJ) published today regarding Pradaxa® (dabigatran etexilate), as we are concerned that the reporting might put patients at risk of stopping their important stroke preventing medication.

On May 13, 2014, in one of the largest real-world analyses of its kind, the U.S. Food and Drug Administration (FDA) once again reaffirmed the positive efficacy-safety profile of Pradaxa® when it issued results from this study in clinical practice. This included more than 134,000 patients, who were 65 years or older and were not monitored.¹

Many of the allegations made by BMJ were reported months ago in the media and have been [previously addressed](#) in full by Boehringer Ingelheim.²

Our company has provided regulators with the complete data set and analyses of clinical evidence demonstrating the efficacy and safety profile of Pradaxa, and FDA and European Medicines Agency (EMA) have affirmed RE-LY's conclusions and stated that Pradaxa® provides an important health benefit when used as directed.^{1,3,4}

BMJ did not put this information into proper context, as their articles do not adequately communicate how crucial it is for patients with atrial fibrillation at risk of stroke to protect themselves from a potentially devastating or even fatal stroke.⁵

Contrary to the BMJ's accusation that Boehringer Ingelheim withheld analyses, here are the facts:

RE-LY® showed Pradaxa® to be a breakthrough for improving stroke prevention versus standard of care.^{6,7} In 2012, our scientists performed preliminary, exploratory simulations with mathematical models to understand whether dose adjustments based on plasma concentrations might further improve the efficacy and safety profile of Pradaxa®. The initial hypothesis from this mathematical model could not be supported when applied to the actual clinical data from the RE-LY® population. Therefore, they were not provided to regulators.

The totality of scientific evidence does not support dosing decisions for Pradaxa® based solely on blood levels. The research shows that individual patient characteristics, such as age, kidney function and certain medications, are critical factors in contributing to the risk of bleeding.

"Boehringer Ingelheim made a robust effort to try and find ways to utilize plasma levels to further improve the efficacy and safety profile of Pradaxa® and it is wrong to suggest otherwise. The truth is, if these approaches could have been developed, we would have used them to the benefit of patients," said Klaus Dugi, Chief Medical Officer, Boehringer Ingelheim. "We are convinced of Pradaxa® and this drug is very close to our hearts. It has been calculated that our drug has already prevented more than 130,000 strokes compared to no treatment."



Klaus Dugi

We are deeply concerned that articles like the BMJ's reports could compromise the health and safety of people who currently benefit from Pradaxa®.

The design of the RE-LY® trial, which studied two different doses of Pradaxa® in one trial, was intensively discussed and agreed with regulatory authorities as it was found to be robust and valid. It included more than 18,000 patients in over 40 countries, and is one of the largest trials ever conducted in non-valvular atrial fibrillation patients to assess stroke risk reduction.⁸ Post-market data reinforce the positive efficacy and safety profile shown in RE-LY® in clinical practice.^{1,3,4}

As with any anticoagulant, there needs to be a balanced consideration of stroke risk reduction and bleeding risk. Patients should not stop taking their anticoagulant medication without first talking to their health care providers. Discontinuing anticoagulation therapy puts a patient at increased risk of stroke.

Value through Innovation

25 July 2014

NOTES TO THE EDITORS

The FDA Medicare Study¹

In its ongoing review of Pradaxa®, the FDA completed a new and independent study with more than 134,000 patients, who were 65 years or older. The study compares the drug to the blood thinner warfarin. Results: The risk of myocardial infarction was similar for the two drugs. As in RE-LY®, the study found an increased risk of major gastrointestinal bleeding with use of Pradaxa® as compared to warfarin. But the most important results are that among new users of blood-thinning drugs, Pradaxa® was associated with a lower risk of clot-related strokes, bleeding in the brain, and death, than warfarin.

The analysis was published as an FDA Drug Safety Communication on May 13, 2014 on the FDA website.

About Pradaxa® (dabigatran etexilate)

Clinical experience of Pradaxa® (dabigatran etexilate) exceeds that of all other novel oral anticoagulants, equating to over 3 million patient-years in all licensed indications worldwide. Pradaxa® has been in the market for more than 6 years and is approved in over 100 countries.⁹

Currently approved indications for Pradaxa® are:¹⁰

- Prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation and a risk factor for stroke
- Primary prevention of venous thromboembolic events in patients undergoing elective total hip replacement surgery
- Primary prevention of venous thromboembolic events in patients undergoing elective total knee replacement surgery
- Treatment of DVT and PE and the prevention of recurrent DVT and PE in adults

Additional registration processes for Pradaxa® in the treatment of DVT and PE, and prevention of recurrent DVT and PE, continue in individual countries worldwide.

Pradaxa®, a direct thrombin inhibitor (DTI), was the first widely approved drug in a new generation of direct oral anticoagulants, available to target a high unmet medical need in the prevention and treatment of acute and chronic thromboembolic diseases.^{11,12} Potent antithrombotic effects are achieved with direct thrombin inhibitors by specifically blocking the activity of thrombin, the central enzyme in the process responsible for clot (thrombus) formation.¹² In contrast to vitamin-K antagonists, which variably act via different coagulation factors, Pradaxa® provides effective, predictable and reproducible anticoagulation with a low potential for drug-drug interactions and no drug-food interactions, without the need for routine coagulation monitoring or mandatory dose adjustment.^{11,13}

Boehringer Ingelheim

The Boehringer Ingelheim group is one of the world's 20 leading pharmaceutical companies. Headquartered in Ingelheim, Germany, Boehringer Ingelheim operates globally with 142 affiliates and a total of more than 47,400 employees. The focus of the family-owned company, founded in 1885, is researching, developing, manufacturing and marketing new medications of high therapeutic value for human and veterinary medicine.

Taking social responsibility is an important element of the corporate culture at Boehringer Ingelheim. This includes worldwide involvement in social projects, such as the initiative "Making more Health" and caring for the employees. Respect, equal opportunities and reconciling career and family form the foundation of the mutual cooperation. In everything it does, the company focuses on environmental protection and sustainability.

In 2013, Boehringer Ingelheim achieved net sales of about 14.1 billion euros. R&D expenditure corresponds to 19.5% of its net sales.

References

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