Press Release

For non-US Healthcare Media

US FDA Approves Pradaxa® (dabigatran etexilate) – a breakthrough treatment for stroke risk reduction in non-valvular atrial fibrillation

Ingelheim, Germany, October 20, 2010 – The US Food and Drug Administration (FDA) has approved Pradaxa® (dabigatran etexilate),1 Boehringer Ingelheim’s novel, oral direct thrombin inhibitor2 for stroke risk reduction in patients with non-valvular atrial fibrillation (AF) marking the first approval of a new oral anticoagulant in the U.S. in more than 50 years. The approval makes Pradaxa® available to a broad spectrum of patients, with the 150 mg bid dose approved for all patients except for a small subset with severe renal impairment (creatinine clearance 15-30 mL/min) where the approved dose is 75 mg bid.

The approval is based on findings from RE-LY®, the largest AF trial completed to date and is set to provide a breakthrough for stroke prevention in AF. The results demonstrated that dabigatran etexilate 150 mg significantly reduced the risk of stroke and systemic embolism by 35 percent beyond the reduction achieved with warfarin, the longtime standard of care, in addition to reductions in life-threatening and intracranial
Besides providing superior efficacy compared to warfarin, dabigatran etexilate does not require monitoring or related dose adjustments, is not affected by food, and no dose adjustment is required for many common co-medications in AF patients.

Physicians and patients in the US will now be the first to have access to this novel agent for this indication, which has the potential to change the treatment paradigm in stroke prevention in AF.

The RE-LY® trial showed for dabigatran etexilate compared with warfarin:

- Significant reduction in the risk of stroke and systemic embolism – including haemorrhagic strokes with the 150mg bid dose
- Significantly lower major bleeding events with the 110mg bid dose
- Significantly lower life threatening and intracranial bleeding with both doses
- Significant reduction in vascular mortality with the 150mg bid dose.

Dr. Stuart Connolly, co-principal investigator of RE-LY®, Director, Division of Cardiology at McMaster University and member of The Population Health Research Institute, Hamilton, Ontario said, “Warfarin has been the standard therapy for stroke prevention in AF for many years. However, it is a very difficult treatment to use because of its interaction with various drugs, food types and the need for continuous monitoring to ensure that the drug is at the right therapeutic level. Anticoagulant monitoring is particularly burdensome and it is often difficult to maintain therapeutic range with warfarin, which puts patients at a higher risk of stroke or major haemorrhage. The approval of dabigatran etexilate provides for the first time an effective, flexible and convenient treatment option in the U.S., which will be especially important for the large group of patients who currently do not take any treatment because they cannot tolerate or
refuse to take warfarin, or are not adequately controlled under current treatment.”

Well-controlled vitamin K antagonist (VKA) therapy (warfarin), currently used for the prevention of stroke in atrial fibrillation, is highly effective in reducing the risk of stroke by approximately two-thirds, but is associated with an increased risk of bleeding as well as several limitations. Drug-drug and food interactions as well as the requirement for frequent monitoring result in only about 50% of eligible patients receiving VKA therapy with fewer than half of these controlled within the therapeutic INR range.

Professor Andreas Barner, Chairman of the Board of Managing Directors and responsible for the Corporate Board Division Research & Development and Medicine, Boehringer Ingelheim, said, “This first approval of Pradaxa® for Stroke Risk reduction in Atrial Fibrillation in the US marks a new era for stroke prevention in atrial fibrillation. This is an important event in the 125-year history of Boehringer Ingelheim and is a very good example for Boehringer Ingelheim’s approach to provide “value through innovation”, i.e. through innovations in an area with high medical demand. This new treatment will improve the lives of many patients and with preventing stroke, will avoid suffering for a significant proportion of them. We expect that dabigatran etexilate will in the coming months become available to patients with atrial fibrillation in more countries, internationally.”

AF is the most common heart rhythm condition, affecting around 1% of the total population, rising to 10% in people over the age of 80. People with AF are at increased risk of blood clots, which raises stroke risk by five times, with up to three million people worldwide suffering strokes related to AF each year, which tend to be especially severe and disabling, with half of people dying within one year.
Notes to Editors

About RE-LY®

RE-LY® (Randomized Evaluation of Long term anticoagulant therapY) was a global, phase III, randomised trial of 18,113 patients enrolled in over 900 centres in 44 countries, investigating whether dabigatran etexilate (2 blinded doses) is as effective as well controlled warfarin with target INR of 2.0-3.0 for stroke prevention. Patients were followed-up in the study for a median of 2 years with a minimum of 1 year follow-up.

The primary endpoint of the trial was incidence of stroke (including haemorrhagic) or systemic embolism. Secondary outcome measures included all-cause death, incidence of stroke (including haemorrhagic), systemic embolism, pulmonary embolism, acute myocardial infarction, and vascular death (including death from bleeding).

Compared to well controlled warfarin, dabigatran etexilate showed in the trial:\(^3\)

- Significant reduction in the risk of stroke and systemic embolism – including haemorrhagic strokes with dabigatran etexilate 150 mg bid
- Significantly lower major bleeding events with dabigatran etexilate 110 mg bid
- Significantly lower life threatening and intracranial bleeding with both doses
- Significant reduction in vascular mortality with dabigatran etexilate 150 mg bid.

About AF and stroke

A total of 6.3 million people in the US, Japan, Germany, Italy, France, UK and Spain were living with AF in 2007 and this is expected to increase to 7.5 million by 2017 primarily due to the ageing population.\(^14\) Strokes due to AF tend to be severe, with an increased likelihood of death (20%), and disability (60%), with resultant societal costs and burden to the healthcare system.\(^13\) AF alone is associated with a cost of up to €13.5 billion across the European Union.\(^8\)

About dabigatran etexilate

Dabigatran etexilate is at the forefront of a new generation of oral anticoagulants/direct thrombin inhibitors (DTIs)\(^7\) targeting a high unmet medical need in the prevention and treatment of acute and chronic thromboembolic diseases.
Potent antithrombotic effects are achieved with direct thrombin inhibitors by specifically blocking the activity of thrombin (both free and clot-bound), the central enzyme in the process responsible for clot (thrombus) formation. In contrast to vitamin-K antagonists, which variably act via different coagulation factors, dabigatran etexilate provides effective, predictable and consistent anticoagulation with a low potential for drug-drug interactions and no drug-food interactions, without the need for routine coagulation monitoring or dose adjustment.

Dabigatran etexilate has already been approved in 75 countries under the trademark Pradaxa® for the primary prevention of venous thromboembolic events (blood clots) in adults who have undergone elective total hip or elective total knee replacement surgery.

Disclaimer
Dabigatran etexilate is only approved for clinical use in stroke risk reduction in non-valvular atrial fibrillation in the U.S. This information is provided for medical education purposes only.

About the dabigatran etexilate clinical trial programme
Boehringer Ingelheim’s clinical trial program to evaluate the efficacy and safety of dabigatran etexilate encompasses studies in:
- Primary prevention of venous thromboembolism (VTE) in patients undergoing elective total hip and knee replacement surgeries
- Treatment of acute VTE
- Secondary prevention of VTE
- Secondary prevention of cardiac events in patients with acute coronary syndrome (ACS)
- Stroke prevention in atrial fibrillation (AF).

Boehringer Ingelheim
The Boehringer Ingelheim group is one of the world’s 20 leading pharmaceutical companies. Headquartered in Ingelheim, Germany, it operates globally with 142 affiliates in 50 countries and more than 41,500 employees. Since it was founded in 1885, the family-owned company has been committed to researching, developing, manufacturing and marketing novel products of high therapeutic value for human and veterinary medicine.

In 2009, Boehringer Ingelheim posted net sales of 12.7 billion euro while spending 21% of net sales in its largest business segment Prescription Medicines on research and development.

For more information please visit www.boehringer-ingelheim.com
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References
1. U.S. FDA – Pradaxa® Prescribing Information


