Bayer HealthCare

Bayer Pharma AG
13342 Berlin
Germany
Tel. +49 30 468-1111
www.bayerpharma.com

News Release

Not intended for U.S. and UK Media

European Label Update of Bayer's Xarelto® Now Including Guidance for Use in Patients with Atrial Fibrillation Undergoing Cardioversion

Label update based on positive CHMP opinion issued in December 2014

Berlin, January 20, 2015 – Bayer HealthCare today announced the inclusion of specific guidance for doctors treating patients with non-valvular atrial fibrillation (AF) undergoing cardioversion to the European Xarelto® (rivaroxaban) Product Information. This label update provides physicians with important information on the clinical utility of rivaroxaban in patients with AF who require cardioversion and is based on the positive CHMP opinion issued in December 2014. It makes Xarelto the only novel oral anticoagulant with specific label guidance for both early and delayed cardioversion.

"Providing adequate anticoagulation therapy for patients with AF undergoing cardioversion is important. With warfarin, patients will often move in and out of the therapeutic range for optimal anticoagulation often requiring postponement of their procedure or leading to increased risk of thromboembolic events like stroke," said Dr Riccardo Cappato, M.D., Arrhythmia and Electrophysiology Center, University of Milan, IRCCS Policlinico San Donato, San Donato Milanese, Milan, Italy and Co-Principal Investigator of the X-VeRT study. "The Xarelto label update provides physicians with clear guidance for patients with atrial fibrillation undergoing cardioversion. The X-VeRT study showed Xarelto to be an effective and well-tolerated alternative to vitamin K antagonists with a practical advantage over VKAs."

The label update is based on findings from the X-VeRT study, the first prospective trial of a novel oral anticoagulant in 1,504 patients with AF undergoing cardioversion. The results from X-VeRT showed that compared with the use of VKA, rivaroxaban was associated with a numerical reduction in the risk of cardiovascular events of 50 per cent in the composite primary efficacy outcome of stroke, transient ischaemic attack, peripheral embolism, myocardial infarction and cardiovascular death (0.5% vs. 1.0%; risk reduction:

0.50; 95% confidence interval: 0.15-1.73), with a numerically lower risk of major bleeding of 24 per cent in the primary safety outcome (0.6% vs. 0.8%; risk reduction 0.76; 95% confidence interval: 0.21-2.67). The practical advantage of using rivaroxaban was demonstrated by the shorter time to cardioversion compared to VKA, particularly in patients scheduled for delayed cardioversion. The study, published in the *European Heart Journal* in September 2014, was designed to supplement previous findings of rivaroxaban from ROCKET AF and was not powered for statistical significance.

About Cardioversion in Patients with AF

Patients with AF experience an irregular heartbeat which causes turbulent blood flow that can lead to the formation of blood clots. Cardioversion is a common medical procedure undertaken to restore the heartbeat from AF back to its regular sinus rhythm. Without adequate anticoagulation, these patients are at risk of thromboembolic complications, with stroke rates of 5-7 per cent. Current guidelines recommend at least three weeks of effective anticoagulation with VKAs (target INR 2.0-3.0) prior to cardioversion (or less if a transesophageal echocardiogram has revealed no thrombus in the left atrial or left atrial appendage) and four weeks of oral anticoagulation after the procedure.

About the X-VeRT Study

X-VeRT was a prospective, randomised, open-label, parallel group Phase IIIb study involving 1,504 patients with hemodynamically stable non-valvular atrial fibrillation of > 48 hours or unknown duration, recruited from 16 countries. Anticoagulation naïve or experienced patients scheduled for cardioversion were randomly assigned to rivaroxaban 20mg once daily (15mg once daily if creatinine clearance was between 30 and 49 mL/min) or INR-adjusted VKA therapy (target INR 2.0-3.0) in a 2:1 ratio. The decision regarding early cardioversion (a goal of between 1–5 days of rivaroxaban or usual VKA therapy before the procedure) or delayed cardioversion (rivaroxaban or VKA for 3-8 weeks prior to the procedure) was taken by the local investigator.

The X-VeRT study contributes to the extensive investigation program of rivaroxaban. After its completion, the program will include more than 275,000 patients in clinical trials and real world settings.

About Xarelto® (Rivaroxaban)

Rivaroxaban is the most broadly indicated novel oral anticoagulant and is marketed under the brand name Xarelto®. Xarelto is approved for five indications across seven distinct

areas of use, protecting patients across more venous and arterial thromboembolic (VAT) conditions than any other novel oral anticoagulant:

- The prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (AF) with one or more risk factors
- The treatment of deep vein thrombosis (DVT) in adults
- The treatment of pulmonary embolism (PE) in adults
- The prevention of recurrent DVT and PE in adults
- The prevention of venous thromboembolism (VTE) in adult patients undergoing elective hip replacement surgery
- The prevention of VTE in adult patients undergoing elective knee replacement surgery
- The prevention of atherothrombotic events (cardiovascular death, myocardial infarction or stroke) after an Acute Coronary Syndrome in adult patients with elevated cardiac biomarkers and no prior stroke or transient ischaemic attack (TIA) when co-administered with acetylsalicylic acid (ASA) alone or with ASA plus clopidogrel or ticlopidine

Whilst licences may differ from country to country, across all indications Xarelto is approved in more than 125 countries.

Rivaroxaban was discovered by Bayer HealthCare, and is being jointly developed with Janssen Research & Development, LLC. Xarelto is marketed outside the U.S. by Bayer HealthCare and in the U.S. by Janssen Pharmaceuticals, Inc. (a Johnson & Johnson Company).

Anticoagulant medicines are potent therapies used to prevent or treat serious illnesses and potentially life-threatening conditions. Before initiating therapy with anticoagulant medicines, physicians should carefully assess the benefit and risk for the individual patient.

Responsible use of Xarelto is a very high priority for Bayer, and the company has developed a Prescribers Guide for physicians and a Xarelto Patient Card for patients to support best practice.

To learn more, please visit https://prescribe.xarelto.com
To learn more about thrombosis, please visit www.thrombosisadviser.com
To learn more about Xarelto, please visit www.xarelto.com

About Bayer HealthCare
The Bayer Group is a global enterprise with core competencies in the fields of health care, agriculture and high-tech materials. Bayer HealthCare, a subgroup of Bayer AG with annual sales of EUR 18.9 billion (2013), is one of the world's leading, innovative companies in the healthcare and medical products industry and is based in Leverkusen, Germany. The company combines the global activities of the Animal Health, Consumer Care, Medical Care and Pharmaceuticals divisions. Bayer HealthCare's aim is to discover, develop, manufacture and market products that will improve human and animal health worldwide. Bayer HealthCare has a global workforce of 56,000 employees (Dec 31, 2013) and is represented in more than 100 countries. More information is available at www.healthcare.bayer.com

Our online press service is just a click away: press.healthcare.bayer.com

Contact:
Astrid Kranz, Tel. +49 30 468-12057
E-Mail: astrid.kranz@bayer.com

Daniela Esser, Tel. +49 30 468-15805
E-Mail: daniela.esser@bayer.com

Find more information at www.bayerpharma.com.
sp (2015-0002E)