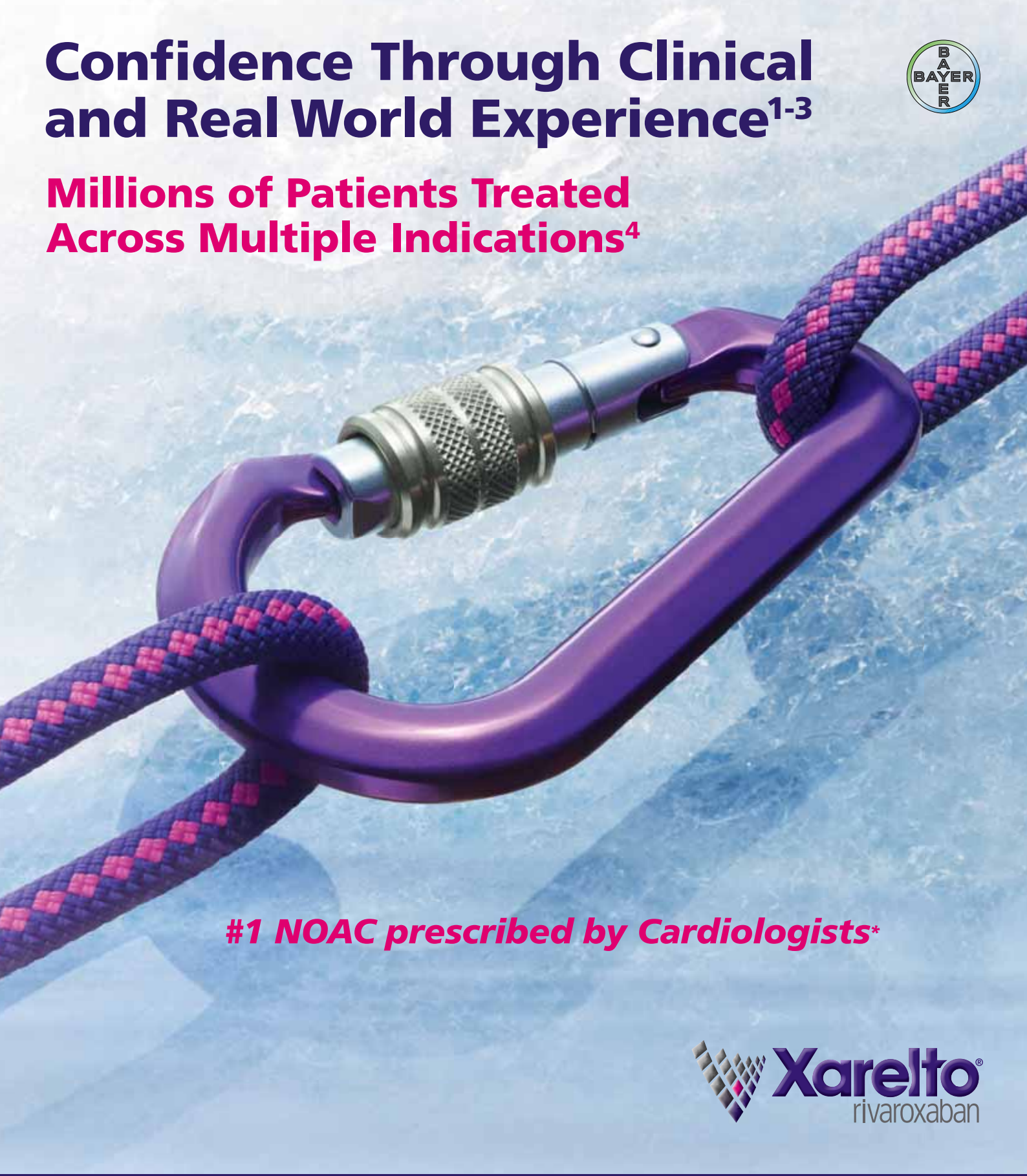
Confidence Through Clinical and Real World Experience[1-3]

Millions of Patients Treated Across Multiple Indications[4]



#1 NOAC prescribed by Cardiologists*

Xarelto® rivaroxaban

References:

1. Patel M.R., Mahaffey K.W., Garg J. *et al.* Rivaroxaban versus warfarin in non-valvular atrial fibrillation. *N Engl J Med.* 2011;365(10):883–91.

2. Tamayo S., Peacock W.F., Patel M.R., *et al.* Characterizing major bleeding in patients with nonvalvular atrial fibrillation: A pharmacovigilance study of 27 467 patients taking rivaroxaban. *Clin Cardiol.* 2015;38(2):63–8. **3.** Camm A.J., Amarenco P., Haas S. *et al.* XANTUS: A Real-World, Prospective, Observational Study. **4.** Calculation based on IMS Health MIDAS, Database: Monthly Sales December 2015.

HCR: Bayer (Pty) Ltd, Reg. No.: 1968/011192/07, 27 Wrench Road, Isando, 1609. Tel: 011 921 5044 Fax: 011 921 5041.

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*Impact RX Data Oct - Dec 2015

NOAC: Non Vitamin K Oral Anticoagulant

EMA REAFFIRMS POSITIVE BENEFIT-RISK BALANCE OF BAYER'S XARELTO® FOR STROKE PREVENTION IN PATIENTS WITH ATRIAL FIBRILLATION

JOHANNESBURG, 18 FEBRUARY 2016

The European Medicines Agency (EMA) has reaffirmed the positive benefit-risk balance of Bayer's Xarelto® (rivaroxiban) for stroke prevention in patients with non-valvular atrial fibrillation. This outcome concludes a CHMP (Committee for Medicinal Products for Human Use) procedure that was initiated to assess whether a potential malfunctioning of the INR device used in the ROCKET AF trial had any impact on the study results. Bayer and its development partner, Janssen, have undertaken thorough analyses, which were shared with most Health Authorities, in particular EMA and the FDA. The EMA has concluded that a defect with the INR device used in the ROCKET study does not change its conclusions on the overall safety or benefit-risk balance of Xarelto (rivaroxaban). In particular, the EMA in their announcement states that "after further analyses of the ROCKET study data (taking into account the defect in the INR device) concluded that any incorrect measurements obtained with the defective device would have had only a marginal effect on the study results, and the safety of Xarelto remains unchanged. Data from other large studies confirmed the comparative safety of the medicine and showed similar rates of bleeding in their warfarin groups." The EMA therefore states: "This means that Xarelto can continue to be used as before, in line with the current prescribing information." "As a member of the ROCKET AF Executive Committee, but equally important as a physician, the re-analysis provides me with additional confidence in the strength and robustness of the ROCKET AF trial. It is valuable to be able to provide reassurance to my fellow colleagues but also to our patients and their carers about the evidence for the benefits of rivaroxaban in protecting people with atrial fibrillation from the risk of a stroke," said Professor Keith A. A. Fox, Duke of Edinburgh Emeritus Professor of Cardiology of the University of Edinburgh, Scotland and Member of the ROCKET AF Executive Committee. "We are very pleased with EMA's assessment confirming the positive benefit-risk profile of Xarelto for stroke prevention in patients with atrial fibrillation," said Dr Michael Devoy, Head of Medical Affairs & Pharmacovigilance of Bayer AG's Pharmaceuticals Division and Bayer Chief Medical Officer.

When Bayer and Janssen became aware of the device correction notice and that the devices used in ROCKET AF should have been included in the device correction notice, in September 2015, they proactively and quickly notified most of the leading health authorities around the world and conducted a number of analyses to assess any potential impact on the primary efficacy and safety results of the ROCKET AF clinical trial. These analyses confirm the results of the ROCKET AF study and the positive benefit-risk profile of Xarelto in patients with non-valvular atrial fibrillation. Xarelto is an important anticoagulant used to treat and reduce the risk of life-threatening blood clots. Beyond ROCKET AF, the companies have evaluated the performance of Xarelto in more than 91 000 patients across its approved indications in real-world research following the medicine's approval, and study after study continues to confirm that Xarelto is performing as expected with a positive benefit-risk profile. This is further supported by evidence generated through independent post-marketing studies conducted by regulators and clinicians as well as the study XANTUS which investigated the use of Xarelto in more than 6 700 patients with AF for stroke prevention in routine clinical practice.

ABOUT XARELTO® (RIVAROXABAN)

Rivaroxaban is the most broadly indicated non-vitamin K antagonist oral anticoagulant (NOAC) and is marketed under the brand name Xarelto®. Xarelto is approved for seven indications, protecting patients across more venous and arterial thromboembolic (VAT) conditions than any other NOAC:

- 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 lower limb surgery

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.