Investor News

Not intended for U.S. and UK Media

New guidelines from the European Society of Cardiology (ESC):

Xarelto™ 2.5 mg plus aspirin recommended for patients at high risk of heart attacks, strokes and death due to chronic coronary syndromes

- Clinical practice guidelines from the European Society of Cardiology (ESC) recommend Xarelto vascular dose (2.5 mg twice daily) plus aspirin low dose once daily in the management of patients with chronic coronary syndromes (CCS) as well as for patients with diabetes and lower extremity arterial disease
- New guidelines include a change in nomenclature from '*stable* coronary artery disease' to '*chronic* coronary syndromes' to better reflect the continuous high risk of heart attacks, strokes and death within this patient population

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Leverkusen, Germany, September 2, 2019 – The European Society of Cardiology (ESC) has published new clinical practice guidelines on the management of diabetes and 'chronic coronary syndromes (CCS)', which replace the 2013 recommendations for the management of stable coronary artery disease (CAD). The guidelines now recommend that treatment with Xarelto vascular dose (2.5 mg twice daily) plus aspirin low dose once daily should be considered in the treatment of patients with chronic coronary syndromes at high risk of further events and low risk of bleeding. Another new ESC guideline adressing diabetes also includes such a recommendation for this regimen in patients with diabetes and lower extremity arterial disease. A new analysis of the COMPASS study published in the *Journal of the American College of Cardiology* in July this year has demonstrated that patients with high risk factors benefited most from dual pathway inhibition with Xarelto and aspirin.

Professor John Eikelboom, Associate Professor, Division of Hematology & Thromboembolism, Department of Medicine, McMaster University, Canada, said: "Chronic coronary syndromes remain a leading cause of morbidity and mortality

worldwide. It´s a progressive condition that is never stable. Adding new treatment recommendations, including the Class IIa recommendation for Xarelto in combination with aspirin, to the updated ESC clinical practice guidelines is therefore a significant step forward in the management of CCS and increases opportunities for patients to benefit from new treatment options."

Adding a second antithrombotic drug like Xarelto vascular dose to aspirin is now recommended for patients with multi vessel CAD with at least one of the following risk factors: peripheral arterial disease (PAD), recurrent myocardial infarction, diabetes mellitus requiring medication or chronic kidney disease (CKD). It is also recommended for patients with a previous myocardial infarction who are at high risk of ischaemic events and have a low risk of bleeding.

In patients with diabetes and chronic symptomatic lower extremity arterial disease - which represents the majority of patients with PAD - without high bleeding risk, the combination of Xarelto vascular dose and aspirin should be considered. The ESC guidelines on CCS and diabetes are the first international guidelines to recommend Xarelto vascular dose plus aspirin.

The new guidelines also include a change in nomenclature from stable coronary artery disease to CCS. The change reflects the reality that these patients with CCS are at continuous risk for heart attacks and strokes. The underlying disease status of coronary artery disease, atherosclerotic plaque accumulation, is a dynamic process that can lead to life threatening thrombotic events including strokes and heart attacks, which remain the main cause of death worldwide.

This recommendation is based on data from the Phase III COMPASS study, which showed that rivaroxaban vascular dose plus aspirin 100 mg once daily reduced the composite risk of stroke, cardiovascular death and heart attack by 24% (relative risk reduction) compared with aspirin 100 mg once daily alone in patients with CAD or PAD[1], including a 42% relative risk reduction in stroke and an 18% mortality reduction. The Phase III randomized controlled COMPASS study was published in 2017, after it was stopped one year ahead of schedule due to overwhelming efficacy.

A new analysis of the COMPASS study published in the *Journal of the American College of Cardiology* in July this year demonstrated that the protection provided by Xarelto

vascular dose plus aspirin 100 mg once daily is especially pronounced in patients with at least one of the following risk factors: involvement of two or more vascular beds, diabetes, renal impairment or a history of heart failure. These patients had a 2-fold increase in vascular events when compared to those individuals without these risk factors.

“We are pleased to see that the ESC recognizes the benefits that adding Xarelto 2.5 mg twice daily on top of aspirin can bring to patients and included the treatment in its updated 2019 guidelines just two years after the COMPASS study was published,” said Dr Michael Devoy, Head of Medical Affairs & Pharmacovigilance of Bayer AG’s Pharmaceuticals Division and Chief Medical Officer. “The vascular dose (Xarelto 2.5 mg twice daily) plus aspirin provides us with a major opportunity to change clinical practice and better treat patients suffering from CAD and/or PAD”.

The guidelines also emphasize the crucial role of healthy lifestyle behaviors, medication and other preventive actions in decreasing the risk of subsequent cardiovascular events and mortality.

About Xarelto™

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 eight 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 pulmonary embolism (PE) in adults
- The treatment of deep vein thrombosis (DVT) in adults
- The prevention of recurrent PE and DVT 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 (CV) death, myocardial infarction (MI) 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

- The prevention of atherothrombotic events in adult patients with coronary artery disease (CAD) or symptomatic peripheral artery disease (PAD) at high risk for ischaemic events when co-administered with acetylsalicylic acid

Xarelto is approved in more than 130 countries, whilst the approved labeling, including the number of indications may differ from country to country.

Rivaroxaban was discovered by Bayer, and is being jointly developed with Janssen Research & Development, LLC. Xarelto is marketed outside the U.S. by Bayer and in the U.S. by Janssen Pharmaceuticals, Inc. (Janssen Research & Development, LLC and Janssen Pharmaceuticals, Inc. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson).

Anticoagulant medicines are potent therapies used to prevent or treat serious illnesses and potentially life-threatening conditions. Before initiating treatment 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 about thrombosis, please visit www.thrombosisadviser.com
To learn more about Xarelto, please visit www.xarelto.com

About Bayer

Bayer is a global enterprise with core competencies in the life science fields of health care and nutrition. Its products and services are designed to benefit people by supporting efforts to overcome the major challenges presented by a growing and aging global population. At the same time, the Group aims to increase its earning power and create value through innovation and growth. Bayer is committed to the principles of sustainable development, and the Bayer brand stands for trust, reliability and quality throughout the world. In fiscal 2018, the Group employed around 117,000 people and had sales of 39.6 billion euros. Capital expenditures amounted to 2.6 billion euros, R&D expenses to 5.2 billion euros. For more information, go to www.bayer.com.

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[1] Eikelboom, JW, Connolly SJ, Bosch J, et al. N Engl J Med 2017; 377:1319-1330.