



News Release

UK MEDICAL AND CONSUMER MEDIA

Bayer plc
400 South Oak Way
Reading
RG2 6AD
www.bayer.co.uk

Bayer's rivaroxaban (Xarelto[®] ▼) Provides Superior Protection Against Recurrent Venous Thromboembolism (VTE) Compared to Aspirin

- 10 mg once daily of rivaroxaban reduced relative risk of recurrent VTE by 74% compared with aspirin 100 mg once daily
- Among the 3,396 patients rates of major bleeding (principle safety outcome) comparable between rivaroxaban and aspirin

Reading, UK, March 18, 2017 – Bayer AG and its development partner Janssen Pharmaceuticals, Inc. today announced results from the EINSTEIN CHOICE study showing rivaroxaban (Xarelto[®]) providing superior protection against recurrent venous thromboembolism (VTE) for patients who have completed 6 to 12 months of anticoagulation therapy (for pulmonary embolism or symptomatic deep vein thrombosis) than daily aspirin. The study published in *The New England Journal of Medicine* demonstrated that 10 mg once daily of the oral Factor Xa inhibitor reduced relative risk of recurrent VTE by 74% compared with aspirin 100 mg once daily.

“This data is very significant for clinical practice as it helps to address an important question that arises daily. At the moment due to a lack of robust clinical evidence many doctors are reluctant to continue anticoagulation therapy for longer durations because of uncertainty around the benefit-risk balance,” comments Dr Alexander T. Cohen, Principal study investigator, Guys & St Thomas’ Hospitals, Kings College London. “The findings from EINSTEIN CHOICE demonstrate the benefit of prescribing rivaroxaban for the extended treatment of VTE. Once approved, rivaroxaban 10 mg once daily, alongside the currently approved 20 mg once daily, will provide doctors with an additional weapon in their armamentarium in the battle to reduce the risk of recurrent VTEs, alleviating some of the pressure on our hospitals, reducing VTE-related deaths and improving the quality of life for people who have experienced an unprovoked VTE or are living with ongoing risk factors.”

VTE affects approximately 1 in every 1,000 people in the UK¹ and each year more than 25,000 people in the UK die from VTE². In patients with VTE, anticoagulation therapy is recommended for 3 months or longer, depending on the balance between the risk of recurrent VTE and the risk of bleeding. However, the risk for patients with unprovoked VTE or with ongoing risk factors experiencing a second event is up to 10% in the first year if treatment is stopped³.



News Release

UK MEDICAL AND CONSUMER MEDIA

Bayer plc
400 South Oak Way
Reading
RG2 6AD
www.bayer.co.uk

“The threat of a secondary VTE is very real for people who have stopped receiving treatment after 3, 6 or 12 months. A lot of the men and women we speak to describe a ‘dark cloud’ hanging over them as they fear the worst from the watch and hope for the best approach,” comments Professor Simon Noble, Thrombosis UK. “We welcome the data released today that will enable people who have had an unprovoked VTE, or who are at high risk, to live their lives with more certainty knowing that by receiving extended treatment their risk of a recurrent VTE is significantly reduced.”

Dr Luis Felipe Graterol, Medical Director, Bayer UK, said: “We are excited to see results that have such important implications for daily clinical practice. This reinforces our long-term commitment to cardiovascular health across both our current and future indications to help support better care and outcomes for people with cardiovascular disease in the UK. Bayer has a robust heritage in addressing unmet needs in cardiovascular health, and a strong pipeline of new indications that we hope will make a real difference in everyday clinical practice.”

Data from the EINSTEIN CHOICE study also demonstrated that rivaroxaban 20 mg once daily (already approved treatment regimen) significantly reduced the relative risk of recurrent VTE by 66% compared with aspirin 100 mg once daily. Furthermore, among the 3,396 patients, rates of major bleeding (principle safety outcome) were comparable and very low across all three treatment arms (0.5% for rivaroxaban 20 mg once daily, 0.4% for rivaroxaban 10 mg once daily, and 0.3% for aspirin 100 mg once daily). Importantly, the study did not include patients with a definitive need for ongoing anticoagulation treatment beyond an initial 6 to 12 month period.

Results from EINSTEIN CHOICE were presented today as a Late-Breaking Clinical Trial at the American College of Cardiology (ACC) 66th Annual Scientific Session in Washington DC and were simultaneously published in *The New England Journal of Medicine*. Data from EINSTEIN CHOICE have been submitted to the European Medicines Agency (EMA) and will be submitted to other Health Authorities including the FDA during the first half of 2017.



News Release

UK MEDICAL AND CONSUMER MEDIA

Bayer plc
400 South Oak Way
Reading
RG2 6AD
www.bayer.co.uk

Reporting of side effects:

This medicine is subject to additional monitoring ▼. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See www.mhra.gov.uk/yellowcard for how to report side effects.

ENDS

About EINSTEIN CHOICE

EINSTEIN CHOICE was a randomised, double-blind, superiority study comparing the efficacy and safety of two doses of rivaroxaban (10 mg once daily and 20 mg once daily) with aspirin (100 mg once daily) for the extended treatment of VTE for up to one year in patients with objectively confirmed PE or symptomatic DVT who had previously completed 6 to 12 months of anticoagulation therapy⁴. Aspirin was chosen as the comparator because aspirin 100 mg once daily has previously been shown to reduce the risk of recurrent VTE by approximately 32% without significantly increasing the risk of serious bleeding when compared with placebo, findings which led to its inclusion in current Guidelines^{5,6,7}.

A total of 3,396 patients were randomised from 244 sites in 31 countries. Importantly, patients with a need for continued therapeutic anticoagulation therapy were not included in the study as the objective of the study was to investigate those patients for whom the treating physician was uncertain about the need for continuing anticoagulation therapy at therapeutic doses⁴.

The primary efficacy outcome was fatal or non-fatal symptomatic recurrent VTE (composite of symptomatic recurrent VTE, VTE-related death and unexplained death for which PE could not be excluded). The principal safety outcome was major bleeding. Only the primary efficacy outcome comparison of rivaroxaban 20 mg vs aspirin and rivaroxaban 10 mg vs aspirin was powered for superiority⁴.

EINSTEIN CHOICE demonstrated that rivaroxaban 20 mg once daily significantly reduced the risk of recurrent VTE by 66% (relative risk reduction) compared with aspirin (1.5% vs 4.4%; HR 0.34; 95% CI 0.20-0.59; $p < 0.001$). Rivaroxaban 10 mg once daily significantly reduced the risk of recurrent VTE by 74% (relative risk reduction) compared with aspirin (1.2% vs 4.4%; HR 0.26; 95% CI 0.14-0.47; $p < 0.001$). Rates of major bleeding were comparable and very low across all three treatment arms at rates of 0.5% for rivaroxaban 20 mg once daily, 0.4% for rivaroxaban 10 mg once daily and 0.3% in the aspirin group with 99.6% of patients not experiencing any major bleeding⁴.



News Release

UK MEDICAL AND CONSUMER MEDIA

Bayer plc
400 South Oak Way
Reading
RG2 6AD
www.bayer.co.uk

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 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 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 130 countries.

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 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.

Bayer: Science For A Better Life



News Release

UK MEDICAL AND CONSUMER MEDIA

Bayer plc
400 South Oak Way
Reading
RG2 6AD
www.bayer.co.uk

Bayer is a global enterprise with core competencies in the Life Science fields of health care and agriculture. Its products and services are designed to benefit people and improve their quality of life. At the same time, the Group aims to create value through innovation, growth and high earning power. Bayer is committed to the principles of sustainable development and to its social and ethical responsibilities as a corporate citizen. In fiscal 2016, the Group employed around 115,200 people and had sales of EUR 46.8 billion. Capital expenditures amounted to EUR 2.6 billion, R&D expenses to EUR 4.7 billion. These figures include those for the high-tech polymers business, which was floated on the stock market as an independent company named Covestro on October 6, 2015. For more information, go to www.bayer.com.

Contact:

Hayley Knight, Tel. 01635 563 523

E-Mail: hayley.knight@bayer.com

Jessica Smith, Tel. +44 (0) 20 8939 1294

E-Mail: jessica.smith@virgohealth.com

Forward-Looking Statements

This release may contain forward-looking statements based on current assumptions and forecasts made by Bayer management. Various known and unknown risks, uncertainties and other factors could lead to material differences between the actual future results, financial situation, development or performance of the company and the estimates given here. These factors include those discussed in Bayer's public reports which are available on the Bayer website at www.bayer.com. The company assumes no liability whatsoever to update these forward-looking statements or to conform them to future events or developments.

¹ NHS England. Venous thromboembolism. Available at: <https://www.england.nhs.uk/patientsafety/venous-thromb/> [Last accessed March 2017].

² National Clinical Guideline Centre – Acute and Chronic Conditions. 2010. Venous thromboembolism: reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in patients admitted to hospital.



News Release

UK MEDICAL AND CONSUMER MEDIA

Bayer plc
400 South Oak Way
Reading
RG2 6AD
www.bayer.co.uk

³ Weitz JI, Bauersachs R, Beyer-Westendorf J, et al. Two doses of rivaroxaban versus aspirin for prevention of recurrent venous thromboembolism. Rationale for and design of the EINSTEIN CHOICE study. *Thromb Haemost* 2015;114:645-50.

⁴ Weitz JI, Lensing AWA, Prins M, et al. Rivaroxaban or aspirin for extended treatment of venous thromboembolism (EINSTEIN CHOICE). Late-Breaking Oral Presentation (Session 404) at ACC.17.

⁵ Brighton TA, Eikelboom JW, Mann K, et al. Low-dose aspirin for preventing recurrent venous thromboembolism. *N Engl J Med* 2012;367:1979-87.

⁶ Becattini C, Agnelli G, Schenone A, et al. Aspirin for preventing the recurrence of venous thromboembolism. *N Engl J Med* 2012;366:1959-67.

⁷ Simes J, Becattini C, Agnelli G, et al. Aspirin for the prevention of recurrent venous thromboembolism: the INSPIRE collaboration. *Circulation* 2014;130:1062-71.