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In a Subanalysis, Eliquis® (apixaban) Reduced the Risk of Stroke and Demonstrated Fewer Major Bleeding Events Versus Warfarin Consistently Across Age Groups, Including Older Patients with Nonvalvular Atrial Fibrillation[i]

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Data from Phase 3 ARISTOTLE trial pre-specified subanalysis published in the European Heart Journal

Bristol-Myers Squibb Company (NYSE: BMY) and Pfizer Inc. (NYSE: PFE) today announced results of a pre-specified subanalysis of the Phase 3 ARISTOTLE trial in relation to patient age. ARISTOTLE was designed to evaluate the efficacy and safety of Eliquis compared to warfarin for reducing the risk of stroke or systemic embolism in patients with nonvalvular atrial fibrillation (NVAF). This subanalysis found consistent results across age groups for reducing the risk of stroke and systemic embolism and reducing the risk of all-cause death with fewer bleeding events. Owing to the higher risk at older age (age 75 and older), the absolute benefit to patients with NVAF was greater with Eliquis in the older population. These data were published today in the European Heart Journal.

Eliquis was more effective than warfarin in reducing the risk of stroke and reducing mortality across age groups, and was associated with less major bleeding, less total bleeding and less intracranial hemorrhage, regardless of age. The p-value for interaction across age groups was non-significant ($p>0.11$ for all) for the major outcomes of stroke and systemic embolism, major bleeding, and death, meaning that the results of this subanalysis were consistent with the overall results of the ARISTOTLE trial.

“Patients with atrial fibrillation are at an increased risk of major cardiovascular events such as stroke, and this risk increases substantially with age,” said study lead author Dr. Sigrun Halvorsen, Department of Cardiology, Oslo University Hospital, Norway. “Eliquis has demonstrated superiority versus warfarin for reducing the risk of stroke and all-cause mortality with fewer major bleeding events in patients with NVAF with consistency across age groups, including patients 75 and older and the very elderly over the age of 80.”

Although the ARISTOTLE trial was neither designed nor powered to investigate the differences for safety and efficacy of Eliquis compared to warfarin for individual age groups, a pre-specified subanalysis of the ARISTOTLE trial was performed according to age. The efficacy and safety of Eliquis compared with warfarin were assessed according to age during the 1.8 years median follow-up. Of the trial population, 30 percent were under age 65, 39 percent were 65 to 74 years old and 31 percent were 75 years or older. In the overall ARISTOTLE trial population, the rates of stroke, major bleeding and death were higher in the older age groups ($p<0.001$ for all) across treatment groups.

IMPORTANT SAFETY INFORMATION FOR ELIQUIS

BOXED WARNING: DISCONTINUING ELIQUIS IN PATIENTS WITHOUT ADEQUATE CONTINUOUS ANTICOAGULATION INCREASES RISK OF STROKE. Discontinuing ELIQUIS places patients at an increased risk of thrombotic events. An increased rate of stroke was observed following discontinuation of ELIQUIS in clinical trials in patients with nonvalvular atrial fibrillation. If anticoagulation with ELIQUIS must be discontinued for a reason other than pathological bleeding, coverage with another anticoagulant should be strongly considered.

CONTRAINDICATIONS

- Active pathological bleeding
- Severe hypersensitivity reaction to ELIQUIS (apixaban) (i.e., anaphylactic reactions)

WARNINGS AND PRECAUTIONS

Increased Risk of Stroke with Discontinuation of ELIQUIS: Discontinuing ELIQUIS in the absence of adequate alternative anticoagulation increases the risk of thrombotic events. An increased rate of stroke was observed during the transition from ELIQUIS to warfarin in clinical trials in patients with nonvalvular atrial fibrillation. If ELIQUIS must be discontinued for a reason other than pathological bleeding, consider coverage with another anticoagulant.

Bleeding Risk: ELIQUIS increases the risk of bleeding and can cause serious, potentially fatal bleeding. Concomitant use of drugs affecting hemostasis increases the risk of bleeding including aspirin and other anti-platelet agents, other anticoagulants, heparin, thrombolytic agents, SSRIs, SNRIs, and NSAIDs. Patients should be made aware of signs or symptoms of blood loss and instructed to immediately report to an emergency room. Discontinue ELIQUIS in patients with active pathological hemorrhage. There is no established way to reverse the anticoagulant effect of apixaban, which can be expected to persist for about 24 hours after the last dose (i.e., about two half-lives). A specific antidote for ELIQUIS is not available. Because of high plasma protein binding, apixaban is not expected to be dialyzable. Protamine sulfate and vitamin K would not be expected to affect the anticoagulant activity of apixaban. There is no experience with antifibrinolytic agents (tranexamic acid, aminocaproic acid) in individuals receiving apixaban. There is neither scientific rationale for reversal nor experience with systemic hemostatics (desmopressin and aprotinin) in individuals receiving apixaban. Use of procoagulant reversal agents such as prothrombin complex concentrate, activated prothrombin complex concentrate, or recombinant factor VIIa may be considered but has not been evaluated in clinical studies. Activated charcoal reduces absorption of apixaban thereby lowering apixaban plasma concentrations.

Prosthetic Heart Valves: The safety and efficacy of ELIQUIS has not been studied in patients with prosthetic heart valves and is not recommended in these patients.

ADVERSE REACTIONS

The most common and most serious adverse reactions reported with ELIQUIS (apixaban) were related to bleeding.

DISCONTINUATIONS FOR SURGERY AND OTHER INTERVENTIONS

ELIQUIS should be discontinued at least 48 hours prior to elective surgery or invasive procedures with a moderate or high risk of unacceptable or clinically significant bleeding. ELIQUIS should be discontinued at least 24 hours prior to elective surgery or invasive procedures with a low risk of bleeding or where the bleeding would be noncritical in location and easily controlled.

DRUG INTERACTIONS

Strong Dual Inhibitors of CYP3A4 and P-gp: Inhibitors of CYP3A4 and P-gp increase exposure to apixaban and increase the risk of bleeding. Decrease the dose of ELIQUIS to 2.5 mg twice daily when coadministered with drugs that are strong dual inhibitors of CYP3A4 and P-gp, (e.g., ketoconazole, itraconazole, ritonavir, or

clarithromycin). In patients already taking ELIQUIS at a dose of 2.5 mg twice daily, avoid coadministration with strong dual inhibitors of CYP3A4 and P-gp.

Strong Dual Inducers of CYP3A4 and P-gp: Inducers of CYP3A4 and P-gp decrease exposure to apixaban and increase the risk of stroke. Avoid concomitant use of ELIQUIS with strong dual inducers of CYP3A4 and P-gp (e.g., rifampin, carbamazepine, phenytoin, St. John's wort) because such drugs will decrease exposure to apixaban.

Anticoagulants and Antiplatelet Agents: Coadministration of antiplatelet agents, fibrinolytics, heparin, aspirin, and chronic NSAID use increases the risk of bleeding. APPRAISE-2, a placebo-controlled clinical trial of apixaban in high-risk post-acute coronary syndrome patients treated with aspirin or the combination of aspirin and clopidogrel, was terminated early due to a higher rate of bleeding with apixaban compared to placebo.

PREGNANCY CATEGORY B
There are no adequate and well-controlled studies of ELIQUIS in pregnant women. Treatment is likely to increase the risk of hemorrhage during pregnancy and delivery. ELIQUIS should be used during pregnancy only if the potential benefit outweighs the potential risk to the mother and fetus.

Please see full Prescribing Information including BOXED WARNING and Medication Guide available at www.bms.com.

About ARISTOTLE
The ARISTOTLE study was designed to evaluate the efficacy and safety of Eliquis versus warfarin for the prevention of stroke or systemic embolism. In ARISTOTLE, 18,201 patients were randomized (9,120 patients to Eliquis and 9,081 to warfarin). ARISTOTLE was an active-controlled, randomized, double-blind, multi-national trial in patients with nonvalvular atrial fibrillation or atrial flutter, and at least one additional risk factor for stroke. Patients were randomized to treatment with Eliquis 5 mg orally twice daily (or 2.5 mg twice daily in selected patients, representing 4.7 percent of all patients) or warfarin (target INR range 2.0-3.0), and followed for a median of 1.8 years.

About Atrial Fibrillation
Atrial fibrillation is the most common cardiac arrhythmia (irregular heartbeat). It is estimated that approximately 5.8 million Americans and six million individuals in Europe have atrial fibrillation. The lifetime risk of developing atrial fibrillation is estimated to be approximately 25 percent for individuals 40 years of age or older. One of the most serious medical concerns for individuals with atrial fibrillation is the increased risk of stroke, which is five times higher in people with atrial fibrillation than those without atrial fibrillation. In fact, 15 percent of all strokes are attributable to atrial fibrillation in the U.S. Additionally, strokes due to atrial fibrillation are more burdensome than strokes due to other causes. Atrial fibrillation-related strokes are more severe than other strokes, with an associated 30-day mortality of 24 percent and a 50 percent likelihood of death within one year in patients who are not treated with an antithrombotic.

About Eliquis®
Eliquis® (apixaban) is an oral direct Factor Xa inhibitor. By inhibiting Factor Xa, a key blood clotting protein, Eliquis prevents thrombin generation and blood clot formation. Eliquis is approved to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation in the United States, European Union (which includes 28 member states), Iceland, Norway, Japan and a number of other countries around the world. Eliquis is approved for prevention of venous thromboembolic events (VTE) in adult patients who have undergone elective hip or knee replacement surgery in the European Union (which includes 28 member states), Iceland, Norway, and a number of other countries around the world. Eliquis is not approved for this indication in

the U.S. or Japan.

About the Bristol-Myers Squibb/Pfizer Collaboration
In 2007, Pfizer and Bristol-Myers Squibb entered into a worldwide collaboration to develop and commercialize Eliquis, an oral anticoagulant discovered by Bristol-Myers Squibb. This global alliance combines Bristol-Myers Squibb's long-standing strengths in cardiovascular drug development and commercialization with Pfizer’s global scale and expertise in this field.

About Bristol-Myers Squibb
Bristol-Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information, please visit http://www.bms.com or follow us on Twitter at http://twitter.com/bmsnews.

Pfizer Inc.: Working together for a healthier world™
At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer health care products. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, Pfizer has worked to make a difference for all who rely on us. To learn more, please visit us at www.pfizer.com.
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