Bristol-Myers Squibb and Pfizer Present Observational Real-World Data Analysis on the Effectiveness and Safety of Eliquis® (apixaban) Compared to Warfarin in Select High-Risk Patients with Non-Valvular Atrial Fibrillation

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Bristol-Myers Squibb Company (NYSE:BMY) and Pfizer Inc. (NYSE:PFE) today announced results from an analysis of real-world data pooled from four large U.S. insurance claims databases. Among non-valvular atrial fibrillation (NVAF) patients, Eliquis® (apixaban) was associated with a lower risk of stroke/SE and lower rates of major bleeding compared to warfarin for the overall population as well as for each of the selected high-risk patient sub-populations. The analysis will be presented today at ESC Congress 2017, organized by the European Society of Cardiology, in Barcelona, Spain.

In this real-world analysis, patients with NVAF receiving either Eliquis or other oral anticoagulants were identified through the U.S. Optum, MarketScan, PharMetrics, and Humana databases. The data was pooled after propensity score matching (PSM) was completed within each database. Select high-risk subgroups were stratified by age, CHA2 DS2-VASc or HAS-BLED score, congestive heart failure (CHF), coronary artery disease (CAD), and peripheral artery disease (PAD). The CHA2DS2-VASc score is a method for estimating stroke risk in patients with non-valvular atrial fibrillation, and the HAS-BLED score helps to estimate risk of major bleeding in patients with NVAF. In the subgroup analysis, based upon these variables, Eliquis was associated with lower risk of stroke/SE

and lower rates of major bleeding compared to warfarin after adjustment for confounding factors. It is important to note that Eliquis increases the risk of bleeding and can cause serious, potentially fatal, bleeding.

“Stroke events continue to be a major concern for patients with NVAF as well as their healthcare providers, and these findings supplement Eliquis clinical trial data,” said Christoph Koenen, M.D., MBA, VP, Development Lead, Eliquis, Bristol-Myers Squibb. “This real-world data analysis helps provide insight into how Eliquis fares in patient populations and settings that clinicians commonly see in practice.”

This observational cohort analysis adds to the body of evidence for Eliquis, which notably includes the Phase 3 ARISTOTLE (Apixaban for Reduction In STroke and Other ThromboembоLic Events in Atrial Fibrillation) clinical trial in which the reduction in risk for stroke/SE, the primary efficacy endpoint for ARISTOTLE, was generally consistent for Eliquis compared with warfarin across various patient subgroups.[i] Real-world data analyses cannot be used as stand-alone evidence to validate the efficacy and/or safety of a treatment. Observational real-world studies can only evaluate association and not causality[ii,iii] (please see full methodology and additional limitations, as well as indications and important safety information for Eliquis, later in this press release).

“The global need to address stroke related to NVAF has never been greater, and the Bristol-Myers Squibb-Pfizer Alliance is intentionally focused on helping to reduce the risk of stroke for as many patients as possible among a broad range of patient type scenarios,” said Rory O’Connor, M.D., Chief Medical Officer, Pfizer Internal Medicine. “We believe real-world data analyses via the ACROPOLIS program are helping to advance deeper levels of insight into how different patient demographics, comorbidities and disease severity factor into how Eliquis may impact patient outcomes.”

In this analysis, Eliquis was associated with lower risk of stroke/SE and lower rates of major bleeding across these risk factors compared to warfarin (38,470 propensity score matched pairs), with a mean follow-up of six months.

	Risk Factor	Risk Factor
Stroke/SE (Number of events; Eliquis vs. warfarin)		
Major Bleeding (Number of events; Eliquis vs. warfarin)		

Age

Younger than 65 years old (n=24,411)

75 vs. 114 (HR: 0.73, 95% CI: 0.54-0.98)

122 vs. 252 (HR: 0.52, 95% CI: 0.42-0.65)

65-74 years old (n=21,325)

103 vs. 141 (HR: 0.80, 95% CI: 0.62-1.03)

189 vs. 354 (HR: 0.57, 95% CI: 0.48-0.69)

75 years or older (n=31,204)

216 vs. 354 (HR: 0.62, 95% CI: 0.52-0.73)

442 vs. 697 (HR: 0.65, 95% CI: 0.57-0.73)

HAS-BLED Score

Less than 3 (n=38,264)

101 vs. 144 (HR: 0.73, 95% CI: 0.56-0.94)

210 vs. 366 (HR: 0.59, 95% CI: 0.50-0.70)

3 or greater (n=38,676)

293 vs. 465 (HR: 0.65, 95% CI: 0.56-0.75)

543 vs. 937 (HR: 0.59, 95% CI: 0.53-0.66)

CHA2DS2-VASc Score

0 to 1 (n=12,770)

18 vs. 21 (HR: 0.84, 95% CI: 0.45-1.58)

39 vs. 73 (HR: 0.52, 95% CI: 0.35-0.77)

2 to 3 (n=30,943)

86 vs. 146 (HR: 0.61, 95% CI: 0.47-0.80)

216 vs. 434 (HR: 0.51, 95% CI: 0.44-0.61)

4 or greater (n=33,227)

290 vs. 442 (HR: 0.69, 95% CI: 0.59-0.80)

498 vs. 796 (HR: 0.66, 95% CI: 0.59-0.73)

CHF

Yes (n=18,530)

141 vs. 221 (HR: 0.66, 95% CI: 0.54-0.82)

299 vs. 511 (HR: 0.61, 95% CI: 0.53-0.70)

No (n=58,410)

253 vs. 388 (HR: 0.67, 95% CI: 0.57-0.79)

454 vs. 792 (HR: 0.59, 95% CI: 0.53-0.66)

CAD

Yes (n=30,147)

210 vs. 298 (HR: 0.71, 95% CI: 0.60-0.85)

414 vs. 688 (HR: 0.60, 95% CI: 0.53-0.68)

No (n=46,793)

184 vs. 311 (HR: 0.62, 95% CI: 0.52-0.74)

339 vs. 615 (HR: 0.58, 95% CI: 0.51-0.66)

PAD

Yes (n=11,665)

95 vs. 176 (HR: 0.61, 95% CI: 0.48-0.78)

184 vs. 352 (HR: 0.59, 95% CI: 0.49-0.71)

No (n=65,275)
299 vs. 433 (HR: 0.70, 95% CI: 0.61-0.81)

569 vs. 951 (HR: 0.61, 95% CI: 0.55-0.67)

Methodology This observational, retrospective analysis was conducted in patients aged 18 years and older who initiated Eliquisor warfarin from January 1, 2013 to September 30, 2015. In each database, 1:1 PSM was used to balance age, gender, region, baseline comorbidities, and prescription comedications. Baseline characteristics were balanced with a mean age of 71 years, mean CHA2DS2-VASc score of 3.0 and mean HAS-BLED score of 2.6. After PSM within each database, the resulting patient-specific results were pooled. Cox proportional hazards models were used to estimate the hazard ratios of stroke/SE and major bleeding (identified using the first listed diagnosis of inpatient claims) within one year of therapy initiation for each subgroup. The statistical significance of the interaction between treatment and the specific subgroup(s) was evaluated.

Limitations of Real-World Data Analyses and of the Select High-Risk Patient Sub-Group Analysis Real-world data have the potential to supplement randomized clinical trial data by providing additional information about how a medicine performs in routine medical practice. Real-world data analyses have several limitations. For example, the source and type of data used may limit the generalizability of the results and of the endpoints. Observational real-world studies can only evaluate association and not causality. Due to these limitations, real-world data analyses cannot be used as stand-alone evidence to validate the efficacy and/or safety of a treatment. It is important to note that, at this time, there are no head-to-head clinical trials comparing direct oral anticoagulants.

In this analysis, given the nature of claims data, diagnoses were identified through ICD-9-CM codes, and drug prescriptions were identified through prescription claims. Missing values, coding errors, and lack of clinical accuracy may have introduced bias into the study. Although some of the datasets contain information from different insurance plans that do not overlap at the plan level, others are employer-based claims datasets which may contain duplicate patient records when pooled together; however, the number of such duplicates is likely to be small – based on a published estimate of 0.5 percentiv – and therefore unlikely to have any important effect on results.

About Eliquis

Eliquis (apixaban) is an oral selective Factor Xa inhibitor. By inhibiting Factor Xa, a key blood clotting protein, Eliquis decreases thrombin generation and blood clot formation. Eliquis is approved for multiple indications in the U.S. based on efficacy and safety data from multiple Phase 3 clinical trials. Eliquis is a prescription medicineindicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation (NVAF); for the prophylaxis of deep vein thrombosis (DVT), which may lead to pulmonary embolism (PE), in patients who have undergone hip or knee replacement surgery; for the treatment of DVT and PE; and to reduce the risk of recurrent DVT and PE, following initial therapy.

ELIQUIS Important Safety Information

WARNING: (A) PREMATURE DISCONTINUATION OF ELIQUIS INCREASES THE RISK OF THROMBOTIC EVENTS, (B) SPINAL/EPIDURAL HEMATOMA (A) Premature discontinuation of any oral anticoagulant, including ELIQUIS, increases the risk of thrombotic events. If anticoagulation with ELIQUIS is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant. (B) Epidural or spinal hematomas may occur in patients treated with ELIQUIS who are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long-term or permanent paralysis. Consider these risks when scheduling patients for spinal procedures. Factors that can increase the risk of developing epidural or spinal hematomas in these patients include: use of indwelling epidural catheters concomitant use of other drugs that affect hemostasis, such as nonsteroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, other anticoagulants a history of traumatic or repeated epidural or spinal punctures a history of spinal deformity or spinal surgery optimal timing between the administration of ELIQUIS and neuraxial procedures is not known Monitor patients frequently for signs and symptoms of neurological impairment. If neurological compromise is noted, urgent treatment is necessary. Consider the benefits and risks before neuraxial intervention in patients anticoagulated or to be anticoagulated.

CONTRAINDICATIONS

Active pathological bleeding Severe hypersensitivity reaction to ELIQUIS (e.g., anaphylactic reactions)
WARNINGS AND PRECAUTIONS

Increased Risk of Thrombotic Events after Premature Discontinuation: Premature discontinuation of any oral anticoagulant, including 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

atrial fibrillation patients. If ELIQUIS is discontinued for a reason other than pathological bleeding or completion of a course of therapy, 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 antiplatelet agents, other anticoagulants, heparin, thrombolytic agents, SSRIs, SNRIs, and NSAIDs. Advise patients of signs and symptoms of blood loss and to report them immediately or go 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 at least 24 hours after the last dose (i.e., about two half-lives). A specific antidote for ELIQUIS is not available. Spinal/Epidural Anesthesia or Puncture: Patients treated with ELIQUIS undergoing spinal/epidural anesthesia or puncture may develop an epidural or spinal hematoma which can result in long-term or permanent paralysis. The risk of these events may be increased by the postoperative use of indwelling epidural catheters or the concomitant use of medicinal products affecting hemostasis. Indwelling epidural or intrathecal catheters should not be removed earlier than 24 hours after the last administration of ELIQUIS. The next dose of ELIQUIS should not be administered earlier than 5 hours after the removal of the catheter. The risk may also be increased by traumatic or repeated epidural or spinal puncture. If traumatic puncture occurs, delay the administration of ELIQUIS for 48 hours. Monitor patients frequently and if neurological compromise is noted, urgent diagnosis and treatment is necessary. Physicians should consider the potential benefit versus the risk of neuraxial intervention in ELIQUIS patients. Prosthetic Heart Valves: The safety and efficacy of ELIQUIS have not been studied in patients with prosthetic heart valves and is not recommended in these patients. Acute PE in Hemodynamically Unstable Patients or Patients who Require Thrombolysis or Pulmonary Embolectomy: Initiation of ELIQUIS is not recommended as an alternative to unfractionated heparin for the initial treatment of patients with PE who present with hemodynamic instability or who may receive thrombolysis or pulmonary embolectomy.

ADVERSE REACTIONS

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

TEMPORARY INTERRUPTION 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. Bridging anticoagulation during the 24 to 48 hours after stopping ELIQUIS and prior to the intervention is not generally required. ELIQUIS should be restarted after the surgical or other procedures as soon as adequate hemostasis has been established.

DRUG INTERACTIONS

Strong Dual Inhibitors of CYP3A4 and P-gp: Inhibitors of cytochrome P450 3A4 (CYP3A4) and P-glycoprotein (P-gp) increase exposure to apixaban and increase the risk of bleeding. For patients receiving ELIQUIS doses of 5 mg or 10 mg twice daily, reduce the dose of ELIQUIS by 50% when ELIQUIS is coadministered with drugs that are strong dual inhibitors of CYP3A4 and P-gp (e.g., ketoconazole, itraconazole, ritonavir, or clarithromycin). In patients already taking 2.5 mg twice daily, avoid coadministration of ELIQUIS with strong dual inhibitors of CYP3A4 and P-gp. Strong Dual Inducers of CYP3A4 and P-gp: 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 and increase the risk of stroke and other thromboembolic events. 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 U.S. Prescribing Information, including BOXED WARNINGS and Medication Guide, available at www.bms.com.

Local prescribing information may vary between countries. Please refer to your local Prescribing Information, including details on indications, dosage, and safety.

About ACROPOLIS™ ACROPOLIS™ (Apixaban ExperienCe Through Real-WOrld POpuLatIon Studies) is the Eliquis (apixaban) global real-world data program designed to generate additional evidence from routine clinical practice settings to further inform healthcare decision makers, including healthcare providers and payers. The

ACROPOLIS program will include retrospective, outcomes-based analyses from over 10 databases around the world, including medical records, medical and pharmacy health insurance claims data, and national health data systems.

Analyses of real-world data allow for a broader understanding of patient outcomes associated with Eliquis outside of the clinical trial setting, as well as insight into other measures of healthcare delivery, such as hospitalization and costs.

About ARISTOTLE ARISTOTLE (Apixaban for Reduction In STroke and Other ThromboembоLic Events in Atrial Fibrillation) 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 the Bristol-Myers Squibb/Pfizer Collaboration In 2007, Pfizer and Bristol-Myers Squibb entered into a worldwide collaboration to develop and commercialize apixaban, 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 about Bristol-Myers Squibb, visit us at BMS.com or follow us on LinkedIn, Twitter, YouTube and Facebook.

About 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, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.pfizer.com. In addition, to learn more, please visit us on www.pfizer.com and follow us on Twitter at @Pfizer and @PfizerNews, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

Bristol-Myers Squibb Forward-Looking Statement This press release contains "forward-looking statements" as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding product development. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes and results to differ materially from current expectations. No forward-looking statement can be guaranteed. Forward-looking statements in this press release should be evaluated together with the many uncertainties that affect Bristol-Myers Squibb's business, particularly those identified in the cautionary factors discussion in Bristol-Myers Squibb's Annual Report on Form 10-K for the year ended December 31, 2016, in our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. Bristol-Myers Squibb undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

Pfizer Disclosure Notice The information contained in this release is as of August 28, 2017. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about Eliquis (apixaban), including its potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, the uncertainties inherent in research and development, including, without limitation, the ability to meet anticipated clinical trial commencement and completion dates as well as the possibility of unfavorable clinical trial results, including unfavorable new clinical data and additional analyses of existing clinical data; decisions by regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of Eliquis; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer’s Annual Report on Form 10-K for the fiscal year ended December 31, 2016 and in its subsequent reports on

Form 10-Q, including in the sections thereof captioned “Risk Factors” and “Forward-Looking Information and Factors That May Affect Future Results”, as well as in its subsequent reports on Form 8-K, all of which are filed with the SEC and available at www.sec.gov and www.pfizer.com.

i Granger, CB,Alexander JH, McMurray JJV, et al. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2011;365:981-992. ii Garrison LP, Neumann PJ, Erickson P, Marshall D, Mullins CD. Using real-world data for coverage and payment decisions: the ISPOR real-world data task force report. Value Health. 2007;10:326-335. iii Hannan EL. Randomized clinical trials and observational studies. J Am Coll Cardiol Intv. 2008;1:211-217. iv Broder MS, Neary MP, Chang E, et al. Treatments, complications, and healthcare utilization associated with acromegaly: a study in two large United States databases. Pituitary 2014; 17(4): 333–341.

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