Pfizer Logo

FDA Accepts For Review ELIQUIS® (apixaban) Supplemental New Drug Application For The Treatment Of Deep Vein Thrombosis (DVT) And Pulmonary Embolism (PE), And For The Reduction In The Risk Of Recurrent DVT And PE

Thursday, December 19, 2013 - 12:01pm

Bristol-Myers Squibb Company (NYSE: BMY) and Pfizer Inc. (NYSE: PFE) today announced that the U.S. Food and Drug Administration (FDA) has accepted for review a Supplemental New Drug Application (sNDA) for ELIQUIS® (apixaban) for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and for the reduction in the risk of recurrent DVT and PE. The Prescription Drug User Fee Act (PDUFA) goal date for a decision by the FDA is August 25, 2014.

Together, DVT and PE are known as venous thromboembolism (VTE), and continue to be a major cause of morbidity and mortality, with approximately 900,000 patients in the U.S. and approximately 1 million patients in the EU diagnosed every year.

The sNDA submission is supported by results from two Phase 3 trials, AMPLIFY and AMPLIFY-EXT, which were both originally published in *The New England Journal of Medicine* on June 30, 2013, and December 8, 2012, respectively. AMPLIFY, (**A**pixaban for the initial **M**anagement of **P**u**L**monary embol**I**sm and deep vein thrombosis as First-line therap**Y**), a randomized, double-blind, multicenter trial, included 5,395 patients with confirmed symptomatic DVT or PE requiring treatment for six months, and evaluated ELIQUIS (10 mg twice daily for 7 days followed by 5 mg twice daily thereafter) compared to current standard of care (initial parenteral enoxaparin treatment overlapped by warfarin therapy). AMPLIFY-EXT (**A**pixaban after the initial Management of **P**u**L**monary embol**I**sm and deep vein thrombosis with First-line therap**Y**-**EXT**ended Treatment), a randomized, double-blind, multicenter trial, included 2,486 patients with prior VTE who had completed 6 to 12 months of anticoagulation treatment for DVT or PE. Patients were randomized to receive either ELIQUIS 2.5 mg or 5 mg, or placebo twice daily for 12 months.

Additionally, in November 2013 the European Medicines Agency accepted for review an application for ELIQUIS for the treatment of DVT and PE, and prevention of recurrent DVT and PE.

About Deep Vein Thrombosis and Pulmonary Embolism

Deep vein thrombosis (DVT) is a blood clot in a vein, usually in the leg, that partially or totally blocks the flow of blood. Pulmonary embolism (PE) is a blood clot blocking one or more vessels in the lungs. DVT causes multiple symptoms including pain, swelling and redness and, more importantly, can progress to PE, which carries the risk of sudden death. Together, DVT and PE are known as venous thromboembolism (VTE), and continue to be a major cause of morbidity and mortality, with approximately 900,000 patients in the US and approximately 1 million patients in the EU diagnosed every year. Once a VTE has occurred, up to 10 percent of people may have a VTE recurrence, which could potentially be fatal.

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.

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 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.

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. Among other risks, there can be no guarantee that ELIQUIS *will be approved for these additional indications in the U.S, or, if approved, that these additional indications will lead to increased commercial success. 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, 2012, 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 December 19, 2013. 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. Such risks and uncertainties include, among other things, (i) the uncertainties inherent in research and development; (ii) whether and when ELIQUIS will be approved by the U.S. Food and Drug Administration (FDA) for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) and for the reduction in the risk of recurrent DVT and PE, or by the European Medicines Agency (EMA) for the treatment of DVT and PE and the prevention of recurrent DVT and PE, as well as the FDA's and EMA's decisions regarding labeling and other matters that could affect the availability or commercial potential of those additional indications; (iii) uncertainty regarding the commercial success of those additional indications if they are approved by the FDA and the EMA; and (iv) competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K/A for the fiscal year ended December 31, 2012 and in its reports on Form 10-Q and Form 8-K.

# # # # #

Bristol-Myers Squibb Chrissy Trank (Media) 609-252-3418 christina.trank@bms.com Ranya Dajani (Investors) 609-252-5330 ranya.dajani@bms.com Ryan Asay (Investors) 609-252-5020 ryan.asay@bms.com
Pfizer Inc. Jennifer Kokell (Media) 917-741-4254 jennifer.kokell@pfizer.com Ryan Crowe (Investors) 212-733-8160 ryan.crowe@pfizer.com