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Daiichi Sankyo's Once-Daily Lixiana® (edoxaban) Approved for the Prevention of Stroke and Systemic Embolism in Non-Valvular Atrial Fibrillation and for the Treatment and Prevention of Recurrent Venous Thromboembolism in Switzerland

Tokyo, Japan (April 15, 2015) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) today announced that Swissmedic, the regulatory authority of Switzerland, has granted approval of Lixiana® (edoxaban), an oral, once-daily selective factor Xa inhibitor, for the prevention of stroke and systemic embolism (SE) in adult patients with non-valvular atrial fibrillation (NVAF). Simultaneously, Lixiana® has received marketing authorisation in Switzerland for the treatment of adult patients with venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE), following previous treatment with fractionated or unfractionated heparin for five days, as well as for the prevention of recurrent VTE.[1]

"Lixiana is an important new anticoagulant for physicians and their patients with NVAF and VTE," said Glenn Gormley, MD, PhD, Senior Executive Officer and Global Head of R&D, Daiichi Sankyo Company, Limited and Executive Chairman and President, Daiichi Sankyo, Inc. "The approval of Lixiana in Switzerland marks Daiichi Sankyo's first opportunity to make once-daily edoxaban available in a European country, and illustrates the Company's commitment to providing new treatment options to patients with cardiovascular diseases with significant unmet needs."

The approved indications in Switzerland for Lixiana are based on data from the phase 3 ENGAGE AF-TIMI 48 and Hokusai-VTE studies, the largest and longest single comparative global trials of a novel oral anticoagulant in patients with NVAF or acute VTE, involving 21,105 and 8,292 patients, respectively.[2,3]

In the ENGAGE AF-TIMI 48 study, once-daily edoxaban 60 mg demonstrated non-inferiority to warfarin, for the primary efficacy endpoint of occurrence of stroke or SE in patients with NVAF (1.18% vs. 1.50% per year, respectively; hazard ratio [HR], 0.79; 97.5% confidence interval [CI], 0.63 to 0.99, $p<0.001$). In addition, once-daily edoxaban 60 mg demonstrated a significant 20% risk reduction of major bleeding in patients with NVAF compared to warfarin (2.75% vs. 3.43% per year, respectively; HR, 0.80; 95% CI, 0.71 to 0.91, $p<0.001$).[2]

In the Hokusai-VTE study, once-daily edoxaban 60 mg was non-inferior to warfarin for the primary efficacy endpoint of recurrence of symptomatic VTE (3.2% vs. 3.5% of patients, respectively; HR, 0.89; 95% CI, 0.70 to 1.13, p<0.001). In addition, edoxaban demonstrated a significant 19% risk reduction of clinically relevant bleeding in patients with VTE compared to warfarin (8.5% vs. 10.3% of patients, respectively; HR, 0.81; 95% CI, 0.71 to 0.94, p=0.004).[3]

Atrial fibrillation (AF) is the most common type of heart rhythm disorder, and is associated with substantial morbidity and mortality.[4] More than 80,000 people in Switzerland suffer from AF, and true prevalence may be higher as up to one third of AF patients do not present with symptoms and go undiagnosed.[5] More than six million Europeans are diagnosed with AF, and this figure is expected to at least double over the next 50 years.[6,7] One in five of all strokes are as a result of AF.[6]

VTE is a major cause of morbidity and mortality.[8] VTE is a major health problem in Europe, with over one million VTE events or deaths per year (France, Germany, Italy, Spain, Sweden, UK), including more than 370,000 VTE-related deaths.[8]

About Lixiana (edoxaban)

In Switzerland, Lixiana® (edoxaban) is indicated for the prevention of stroke and SE in adult patients with NVAF, and for the treatment of adult patients with VTE, including DVT and PE, following previous treatment with fractionated or unfractionated heparin for five days, as well as for the prevention of recurrent VTE.[1] The recommended dose of Lixiana is 60 mg once-daily, with a dose reduction to 30 mg once-daily in patients with moderate or severe renal impairment (creatinine clearance [CrCl] 15-50 mL/min), body weight ≤ 60 kg, or concomitant use of certain P-glycoprotein (P-gp) inhibitors (ciclosporin, dronedarone, erythromycin, ketoconazole, quinidine or verapamil).[1]

Edoxaban is currently marketed in Japan and the United States.[9,10] In the EU and other countries, regulatory review is ongoing.

About the ENGAGE AF-TIMI 48 Study

ENGAGE AF-TIMI 48 (**E**ffective a**N**ticoa**G**ulation with factor x**A** next **GE**neration in **A**trial **F**ibrillation) was a three-arm, randomized, double-blind, double-dummy, global phase 3 clinical trial comparing once-daily edoxaban with warfarin in 21,105 patients with NVAF at moderate-to-high risk of thromboembolic events at 1,393 centers in 46 countries. ENGAGE AF-TIMI 48 compared two edoxa-

ban treatment strategies, a higher dose arm (60 mg or 30 mg dose reduced) once-daily and a lower dose arm (30 mg or 15 mg dose reduced) once-daily, with warfarin in patients with NVAF for a median of 2.8 years follow-up. Patients were dose reduced for creatinine clearance (CrCL) 30 to 50 mL/min, body weight of 60 kg or less or certain p-glycoprotein inhibitor use. ENGAGE AF-TIMI 48 represents the largest and longest single comparative global trial with a novel anticoagulant in patients with NVAF performed to date.[2] The full results were presented at the AHA Scientific Sessions 2013 in Dallas and published in the *New England Journal of Medicine.*

About the Hokusai-VTE Study

Hokusai-VTE was a global, event-driven, randomized, double-blind, double-dummy, parallel-group phase 3 clinical study involving 8,292 patients in 439 clinical sites across 37 countries to evaluate once-daily edoxaban in patients with either acute symptomatic DVT, PE or both. The Hokusai-VTE study was designed to reflect clinical practice using a flexible treatment duration of 3-12 months in a broad spectrum of VTE patients, including initial use of parenteral anticoagulant (heparin) for 5-10 days, the proven global standard of care. Patients were randomized to receive edoxaban 60 mg once-daily (dose reduced to 30 mg for CrCL 30 to 50 mL/min, body weight of 60 kg or less, or certain p-glycoprotein inhibitor use) or the comparator, warfarin, following initial open-label enoxaparin or unfractionated heparin therapy. In the comparator arm, patients received initial heparin therapy concurrently with warfarin, titrated to a target INR of 2.0 to 3.0, followed by warfarin alone. The treatment duration was from 3 months and up to a maximum of one year. The duration of study treatment was determined by the investigator based on the patient's clinical features.[3] The full results were presented at the ESC Congress 2013 in Amsterdam and published in the *New England Journal of Medicine*.

About Daiichi Sankyo

Daiichi Sankyo Group is dedicated to the creation and supply of innovative pharmaceutical products to address the diversified, unmet medical needs of patients in both mature and emerging markets. While maintaining its portfolio of marketed pharmaceuticals for hypertension, dyslipidemia and bacterial infections used by patients around the world, the Group has also launched treatments for thrombotic disorders and is building new product franchises. Furthermore, Daiichi Sankyo research and development is focused on bringing forth novel therapies in oncology and cardiovascular-metabolic diseases, including biologics. The Daiichi Sankyo Group has created a "Hybrid Business Model," to respond to market and customer diversity and optimize growth opportunities across the value chain. For more information, please visit: www.daiichisankyo.com.

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Press Release

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Forward-looking statements

This press release contains forward-looking statements and information about future developments in the sector, and the legal and business conditions of DAIICHI SANKYO Co., Ltd. Such forward-looking statements are uncertain and are subject at all times to the risks of change, particularly to the usual risks faced by a global pharmaceutical company, including the impact of the prices for products and raw materials, medication safety, changes in exchange rates, government regulations, employee relations, taxes, political instability and terrorism as well as the results of independent demands and governmental inquiries that affect the affairs of the company. All forward-looking statements contained in this release hold true as of the date of publication. They do not represent any guarantee of future performance. Actual events and developments could differ materially from the forward-looking statements that are explicitly expressed or implied in these statements. DAIICHI SANKYO Co., Ltd. assume no responsibility for the updating of such forward-looking statements about future developments of the sector, legal and business conditions and the company.

References

1. Lixiana® (edoxaban) Prescribing Information. Daiichi Sankyo (Switzerland) AG. 2015.
2. Giugliano R, et al. Edoxaban versus warfarin in patients with atrial fibrillation. *N Engl J Med*. 2013;369(22):2093-2104.
3. Büller H, et al. Edoxaban versus warfarin for the treatment of symptomatic venous thromboembolism. *N Engl J Med*. 2013;369(15):1406-1415.
4. Iqbal MB, et al. Recent developments in atrial fibrillation. *BMJ*. 2005;330(7485):238–43.
5. Pavlovic N, et al. Atrial fibrillation – European and Swiss perspectives. *Cardiovasc Med*. 2014;17(6):167-170.
6. Camm A, et al. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Eur Heart J*. 2010;31(19):2369–2429.
7. Krijthe BP, et al. Projections on the number of individuals with atrial fibrillation in the European Union, from 2000 to 2060. *Eur Heart J*. 2013;34(35):2746-2751.
8. Cohen A, et al. Venous thromboembolism (VTE) in Europe. *Thromb Haemost*. 2007;98(4):756-764.
9. Daiichi Sankyo press release - Daiichi Sankyo Launches New Formulation of LIXIANA® 60 mg Tablets (edoxaban) in Japan. 8 Dec 2014. Available at: http://www.daiichisankyo.com/media_investors/media_relations/press_releases/detail/006226.html. [Last accessed: April 2015.]
10. Daiichi Sankyo press release - SAVAYSA™ (edoxaban) Now Available in U.S. Pharmacies. 9 February 2015. Available at: http://www.daiichisankyo.com/media_investors/media_relations/press_releases/detail/006247.html. [Last accessed: April 2015].