PRESS RELEASE

Once-Daily Anticoagulant LIXIANA® (edoxaban) Approved in Canada for Stroke Prevention in Atrial Fibrillation and for the Treatment and Prevention of Recurrent Deep-Vein Thrombosis and Pulmonary Embolism.

Laval, Quebec (November 9, 2016) – Servier Canada announced today that LIXIANA® (edoxaban) has been approved by Health Canada for the following two indications: prevention of stroke and systemic embolic events in patients with atrial fibrillation, in whom anticoagulation is appropriate and for treatment of venous thromboembolism (VTE) (deep vein thrombosis [DVT], pulmonary embolism [PE]) and the prevention of recurrent DVT and PE.

The approval of LIXIANA® is based on data from two phase 3 trials, ENGAGE AF-TIMI 48 and Hokusai-VTE, which compared treatment with once-daily LIXIANA® to warfarin, a current standard of care for stroke prevention in patients with atrial fibrillation (AF) or for the treatment and prevention of VTE. These studies represent the largest and longest clinical development program for a novel oral anticoagulant (NOAC) in patients with AF or VTE, involving 21,105 and 8,292 patients, respectively.[1,2]

AF affects over 350 000 Canadians and people with AF are at a three to five-fold increased risk of stroke compared to the general population[3] with an estimated financial burden of over 3.6 billion a year.[4] VTE also represents a major cause of morbidity and mortality, with a 30-day mortality rate of 10% and 1-year mortality rate of 23%.[5]

“AF and VTE are two common and debilitating diseases, which have major consequences for the patients and their families. The data behind the two phase 3 trials that led to the approval of LIXIANA® in Canada are robust and LIXIANA® represents an important step forward in the treatment of these two conditions. I am confident that having LIXIANA® in our armamentarium of anticoagulants will help us better manage our patients with AF and VTE”, said Dr. Jeffrey Weitz, Professor of Medicine and Biochemistry at McMaster University, Executive Director of the Thrombosis and Atherosclerosis Research Institute and hematologist at Hamilton Health Sciences.

“Health Canada’s approval provides another treatment option to physicians and patients in need of anticoagulation treatment. LIXIANA® is a convenient only once daily novel anticoagulant that has shown to protect from stroke and systemic embolic events (SEE) as well as warfarin, while being associated with less major bleeding than well-managed warfarin, across a broad range of Atrial Fibrillation (AF) patients” said Dr Paul Dorian, Professor of Medicine and Director, division of Cardiology at University of Toronto and cardiac electrophysiologist at the St-Michael’s hospital.

In the ENGAGE AF-TIMI 48 study[1], once-daily LIXIANA® versus warfarin demonstrated in a broad range of AF patients:

- Similar efficacy for the reduction of stroke and SEE (*p* value for noninferiority <0.001).
- Superior safety with less major bleedings (relative risk reduction (RRR) of 20%, p<0.001).

In the Hokusai-VTE study[2], once daily LIXIANA® versus warfarin demonstrated across a broad range of VTE patients:

- Similar efficacy in the reduction of the symptomatic recurrence of VTE, including DVT and fatal and non-fatal PE (*p* value for noninferiority <0.001).
- Superior safety with less major or clinically relevant nonmajor bleeding (RRR 19%, p=0.004).

''We look forward to making LIXIANA® available to Canadian patients. LIXIANA® is a new treatment option for patients suffering from atrial fibrillation and venous thromboembolism. Servier Canada is committed to working closely with the medical and scientific community to improve the diagnosis and management of these serious conditions. We are very proud to continue to reinforce our long-standing presence in the field of cardiovascular health'' underlined Frederic Fasano, Chief Executive Officer of Servier Canada.

About LIXIANA® (edoxaban)

LIXIANA® (edoxaban) is an oral, direct factor Xa inhibitor. Factor Xa is one of the key components responsible for blood clotting. Atrial fibrillation (AF), a heart rhythm disorder causing irregular rapid contractions of the upper chambers of the heart can lead to the formation of a clot. VTE, another condition in which clots form in deep veins of the leg and break off and travel to the lungs. LIXIANA® prevents the formation of clots in the arteries and veins to prevent stroke, DVT, PE and other end organ damage.

Edoxaban was discovered and developed by Daiichi Sankyo Co., Ltd. On June 27, 2016, Daiichi Sankyo and Servier Canada entered into an agreement whereby Servier Canada would market the oral, once-daily anticoagulant edoxaban in Canada, upon approval by the Canadian health authority. Edoxaban has been approved in the U.S., EU, Switzerland, Japan, South Korea, Taiwan and Hong Kong. Edoxaban is marketed as SAVAYSA® in the U.S. and as LIXIANA® elsewhere.

About Servier Canada

Servier Canada Inc., headquartered in Laval, Quebec, is an affiliate of Servier Group. It is the third largest operation for Servier, and it belongs to the top 20 research-based pharmaceutical companies in Canada. Servier Canada is currently marketing three cardiovascular medicines and is expecting further approvals in the upcoming months. The mission of Servier Canada is to provide the Canadian medical community and their patients with innovative therapeutic solutions in the following therapeutic areas: cardiovascular, diabetes and oncology. Servier Canada collaborates with various stakeholders including researchers, biotech entrepreneurs and innovators. In addition to these partnerships, the Center of

Excellence in Clinical Research of Servier Canada is dedicated to clinical development with more than 50 trials conducted throughout Canada in the last 10 years. More information is available at www.servier.ca

Servier CANADA Media Contact
Nadine Doucet
Servier Canada Inc.
(450) 978-9700 Ext: 4225
nadine.doucet@servier.com

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