

Press Release

Daiichi Sankyo, Inc. Announces New Subgroup Analyses of Once-Daily SAVAYSA® in Patients with Non-Valvular Atrial Fibrillation Will Be Presented at AHA Scientific Sessions 2015

- *Four abstracts highlight new subgroup analyses from the global phase 3 study, ENGAGE AF-TIMI 48*

Parsippany, NJ (November 2, 2015) – Daiichi Sankyo, Inc. today announced that data from four new subgroup analyses from the phase 3 ENGAGE AF-TIMI 48 study will be presented at the American Heart Association (AHA) Scientific Sessions 2015, taking place from November 7-11, 2015, in Orlando, Florida. Results will provide further insights about the safety and efficacy profile of once-daily SAVAYSA® (edoxaban) as compared to warfarin in non-valvular atrial fibrillation (NVAf) patients.

The subgroup analysis data on SAVAYSA will be presented in two oral and two poster sessions. The complete list of presentations is included below:

Presentation Title	Lead Author	Session Details
<i>Oral Sessions</i>		
Gastrointestinal Bleeding with Edoxaban versus Warfarin: Results from the ENGAGE AF-TIMI 48 Trial (AHA Abstract #183)	James Aisenberg, MD, Mount Sinai Hospital, New York, NY	Sunday, November 8 3:45–4:00 PM EST Location: W311CD
The Impact of Renal Function on Outcomes with Edoxaban in the ENGAGE AF-TIMI 48 Trial (AHA Abstract #517)	Erin A. Bohula, MD, DPhil, Brigham and Women's Hospital, Boston, MA	Tuesday, November 10 4:45–5:00 PM EST Location: W206BC

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Poster Sessions

Edoxaban versus Warfarin in Patients with Atrial Fibrillation in the US FDA Approval Population: An analysis from the ENGAGE AF-TIMI 48 trial (AHA Abstract #S4080)	Alon Eisen, MD, Brigham and Women's Hospital, Boston, MA	Sunday, November 8 9:00–10:15 AM EST Location: A2 Clinical Science
Edoxaban versus Warfarin in Patients at Increased Risk of Falling – A Subgroup Analysis of the ENGAGE AF-TIMI 48 trial (AHA Abstract #S4504)	Jan Steffel, MD, University Hospital Zurich, Zurich, Switzerland	Sunday, November 8 2:00–3:15 PM EST Location: A2 Clinical Science

About the ENGAGE AF-TIMI 48 Study

The ENGAGE AF-TIMI 48 global phase 3 study investigated once-daily edoxaban in comparison to warfarin in 21,105 patients with NVAF. This represented the largest and longest trial with a novel oral anticoagulant (NOAC) in patients with atrial fibrillation (AF) performed to date, with a median follow-up of 2.8 years. Edoxaban demonstrated non-inferiority for stroke or systemic embolism (SE) in comparison to warfarin. Edoxaban was also found to be superior for the principal safety endpoint of major bleeding in comparison to warfarin.¹

About Atrial Fibrillation

Atrial fibrillation (AF) is a condition where the heart beats irregularly and rapidly. When this happens, blood can pool and thicken in the chambers of the heart causing an increased risk of blood clots. These blood clots can break off and travel through the blood stream to the brain (or sometimes to another part of the body), where they have the potential to cause a stroke.²

AF is the most common type of heart rhythm disorder, and is associated with substantial morbidity and mortality.³ AF affects approximately 6.1 million people in the U.S.⁴ Compared to those without AF, people with the arrhythmia have a 3-5 times higher risk of stroke.⁵ One in five of all strokes are as a result of AF.⁶

About SAVAYSA® (edoxaban)

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Edoxaban, also known as SAVAYSA in the U.S., is an oral, once-daily anticoagulant that specifically inhibits factor Xa, which is an important factor in the coagulation system that leads to blood clotting. The global edoxaban clinical trial program included two phase 3 clinical studies, Hokusai-VTE and ENGAGE AF-TIMI 48, with nearly 30,000 patients combined. The results from these trials formed the basis of the regulatory filing in the U.S. for SAVAYSA for the reduction in risk of stroke and systemic embolism (SE) in patients with non-valvular atrial fibrillation (NVAF), as well as for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) following 5-10 days of initial therapy with a parenteral anticoagulant. According to the U.S. label, SAVAYSA should not be used in NVAF patients with creatinine clearance (CrCL) levels greater than 95 mL/min because in that population there is an increased risk of ischemic stroke compared to warfarin.^{1,7,8}

Indication

SAVAYSA® (edoxaban) is a prescription medicine used to reduce the risk of stroke and blood clots in people who have atrial fibrillation not caused by a heart valve problem. Based on how well the kidneys work, SAVAYSA may not be a treatment option. Health Care Professionals should check kidney function before starting treatment.

SAVAYSA is used to treat blood clots in the veins of the legs (deep vein thrombosis) or lungs (pulmonary embolism), after treatment with an injectable blood thinner medicine for 5 to 10 days.

Important Safety Information

What is the most important information to know about SAVAYSA?

- **For people who take SAVAYSA for nonvalvular atrial fibrillation (a type of irregular heartbeat):**
 - People with atrial fibrillation are at an increased risk of forming a blood clot in the heart, which can travel to the brain, causing a stroke, or to other parts of the body. SAVAYSA lowers the chance of having a stroke by helping to prevent clots from forming.
 - Health Care Professionals should check kidney function before prescribing SAVAYSA. People whose kidneys work really well should not receive SAVAYSA because it may not work as well as other medications to prevent stroke.
 - Patients should not stop taking SAVAYSA without first talking to their doctor who prescribed it.

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- Stopping SAVAYSA increases the patient's risk of having a stroke.
- **SAVAYSA can cause bleeding which can be serious**, and sometimes lead to death. This is because SAVAYSA is a blood thinner medicine that reduces blood clotting. While taking SAVAYSA, the patient may bruise more easily and bleeding may take longer to stop. Patients should call their doctor or get medical help right away if they experience bleeding that is severe (for example, coughing up or vomiting blood) or bleeding that cannot be controlled.

Patients may have a higher risk of bleeding if they take SAVAYSA and take other medicines that increase their risk of bleeding, including: aspirin, long-term use of nonsteroidal anti-inflammatory drugs (NSAIDs), and blood thinners (warfarin, heparin, or other medicines to prevent or treat blood clots). Patients should tell their doctor if they take any of these medicines. Patients should ask their doctor or pharmacist if they are not sure if their medicine is one listed above.

- **SAVAYSA is not for people with mechanical heart valves or people who have moderate-to severe narrowing (stenosis) of their mitral valve.**
- **Spinal or epidural blood clots (hematoma).** People who take a blood thinner medicine (anticoagulant) like SAVAYSA, and have medicine injected into their spinal and epidural area, or have a spinal puncture have a risk of forming a blood clot that can cause long-term or permanent loss of the ability to move (paralysis). The risk of developing a spinal or epidural blood clot is higher if: a thin tube called an epidural catheter is placed in the patient's back to give him/her certain medicine, the patient takes NSAIDs or a medicine to prevent blood from clotting, the patient has a history of difficult or repeated epidural or spinal punctures, and the patient has a history of problems with his/her spine or have had surgery on his/her spine.
- If a patient takes SAVAYSA and receives spinal anesthesia or has a spinal puncture, the patient's doctor should watch closely for symptoms of spinal or epidural blood clots. Patients should tell their doctor right away if they have back pain, tingling, numbness (especially in the legs and feet), muscle weakness, loss of control of the bowels or bladder (incontinence).

Who should not take SAVAYSA?

Patients should not take Savaysa if they currently have certain types of abnormal bleeding.

What should patients tell their doctor before taking SAVAYSA?

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- Before taking SAVAYSA, patients should tell their doctor if they: have liver or kidney problems, have ever had bleeding problems, have a mechanical heart valve, are pregnant or plan to become pregnant, are breastfeeding or plan to breastfeed.
 - It is not known if SAVAYSA will harm an unborn baby. Patients should tell their doctor right away if they become pregnant during treatment with SAVAYSA.
 - It is not known if SAVAYSA passes into breast milk. Patients should decide with their doctor if they will take SAVAYSA or breastfeed. Patients should not do both.
- Patients should tell all of their doctors and dentists that they are taking SAVAYSA. The healthcare providers should talk to the doctor who prescribed SAVAYSA before the patient has any surgery, medical or dental procedure. Patients should tell their doctor about all the medicines they take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Some other medicines may affect the way SAVAYSA works. Certain medicines may increase the risk of bleeding or stroke when taken with SAVAYSA.

How should the patient take SAVAYSA?

- Patients should take SAVAYSA exactly as prescribed. The doctor will decide how long the patient should take SAVAYSA. The patient should not change their dose or stop taking SAVAYSA unless their doctor tells them to. Patients can take SAVAYSA with or without food. If a dose of SAVAYSA is missed, the patient should take it as soon as he/she remembers that day and not take more than one dose at the same time. The next dose should be taken at the usual time the next day. Patients should not run out of SAVAYSA and should refill their prescriptions before running out.
- If too much SAVAYSA is taken, the patient should go to the nearest hospital emergency room or call his/her doctor right away. Patients should call their doctor right away if they fall or injure themselves, especially if they hit their heads. The doctor may need to check them.

What are the possible side effects of SAVAYSA?

Common side effects in people who take SAVAYSA include, bleeding and low red blood cell count (anemia). Patients should talk to their doctor if they have any side effect that bothers them or that does not go away. Patients should call their doctor for medical advice about side effects. Side effects may be reported to FDA at 1-800-FDA-1088.

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Please see the full Prescribing Information, including Boxed WARNINGS and Medication Guide at savaysa.com.

About Daiichi Sankyo

Daiichi Sankyo Group is dedicated to the creation and supply of innovative pharmaceutical products to address diversified, unmet medical needs of patients in both mature and emerging markets. With over 100 years of scientific expertise and a presence in more than 20 countries, Daiichi Sankyo and its 17,000 employees around the world draw upon a rich legacy of innovation and a robust pipeline of promising new medicines to help people. In addition to its strong portfolio of medicines for hypertension, dyslipidemia, bacterial infections, and thrombotic disorders, the Group's research and development is focused on bringing forth novel therapies in cardiovascular-metabolic diseases, pain management, and oncology, including biologics. For more information, please visit: www.daiichisankyo.com.

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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.

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