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Press Release

Daiichi-Sankyo

UK's NICE recommends once-daily LIXIANA® (edoxaban) for preventing stroke and systemic embolism in patients with non-valvular atrial fibrillation

Tokyo, Japan (September 23, 2015) - The National Institute for Health and Care Excellence (NICE), the medicines cost-effectiveness body for England and Wales, has recommended a new treatment to help prevent stroke and systemic embolism (SE) in patients suffering from the heart rhythm disorder atrial fibrillation (AF).[1]

Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) today announced that NICE has issued its final recommendation for LIXIANA® (edoxaban) for preventing stroke and SE in patients with non-valvular atrial fibrillation (NVAF). This follows NICE's publication of a Final Appraisal Document (FAD) on 6 August 2015, for its Single Technology Appraisal (STA) of LIXIANA for the prevention of stroke and SE in patients with NVAF.[2]

The NICE recommendation comes shortly after LIXIANA received European marketing authorisation in June 2015 for two indications:

- Prevention of stroke and SE in adult patients with NVAF with one or more risk factors, such as congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke or transient ischaemic attack (TIA)
- Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults. The NICE final recommendation for this indication was obtained on 26 August 2015

The final NICE recommendation states: "Edoxaban is recommended, within its marketing authorisation, as an option for preventing stroke and systemic embolism in adults with non-valvular atrial fibrillation with one or more risk factors, including congestive heart failure, hypertension, diabetes, prior stroke or transient ischaemic attack, or age 75 years or older." It adds: "The Committee concluded that taking all of the analyses into account, edoxaban was cost effective compared with warfarin and could be recommended as an alternative to warfarin for preventing stroke and systemic

embolism in people with non-valvular atrial fibrillation who have one or more risk factors for stroke."[1]

Edoxaban, made by the pharmaceutical company Daiichi Sankyo, is one of the class of blood-thinning drugs known as novel oral anticoagulants (NOACs). These drugs are used as an alternative to warfarin, which has been widely used for over 50 years but requires frequent monitoring to ensure the drug is working properly and is also associated with many food and drug interactions.[3]

The final NICE recommendation noted: "The Committee accepted the limitations of warfarin therapy and the considerable impact it may have on people who take it, and recognised the potential benefits of edoxaban for people with non-valvular atrial fibrillation," and concluded that, "edoxaban was as clinically effective as warfarin for the primary efficacy outcome of reducing stroke (ischaemic and haemorrhagic) and systemic embolism, and had nearly half the rate of haemorrhagic stroke events compared to warfarin."[1]

Professor Martin Cowie, Professor of Cardiology at Imperial College London and noted researcher of AF, said edoxaban gives doctors the ability to better tailor medicines to individual patients.

"A few years ago, all we had to prevent strokes in AF patients was warfarin, which imposes many lifestyle restrictions on patients and needs monitoring with a blood test system measuring International Normalised Ratio (INR). Now we have choices with modern blood-thinning drugs that do not need INR monitoring and are easy for patients to live with."

Dr. Simon Clough, UK Managing Director for Daiichi Sankyo, said: "We are very pleased to be able to offer patients and doctors in England and Wales a new convenient alternative in the treatment armoury against AF-related illness. NICE has recognised an unmet clinical need among patients with AF and this recommendation confirms the value of LIXIANA, which combines convenience and safety compared to well managed warfarin with features that patients and physicians appreciate."

AF is the most common type of heart rhythm disorder, and is associated with substantial morbidity and mortality.[4] According to NICE, the estimated prevalence of AF in England is 1.6% of adults aged 18 or over, which equates to approximately 835,000 cases. Of these 835,000 cases, between 476,000 and 702,000 adults could require anticoagulation therapy.[5] In addition, there may be another 250,000

people who are undiagnosed.[6] According to NICE, only an estimated 49.3% of patients with a history of AF are currently receiving anticoagulation therapy.[5]

AF affects approximately 2.3-3.4% of people in developed nations.[7] More than six million Europeans are diagnosed with AF, and this figure is expected to at least double over the next 50 years.[8,9] One in five of all strokes are as a result of AF.[8] Stroke is the second most common cause of death worldwide, responsible for approximately 6.7 million deaths each year.[10]

About AF

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.[11]

About Edoxaban

Edoxaban is an oral, once-daily, direct factor Xa (pronounced “Ten A”) inhibitor. Factor Xa is one of the key components responsible for blood clotting, so inhibiting this makes the blood thin and less prone to clotting.

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 NOAC in patients with AF performed to date, with a median follow-up of 2.8 years.[12] Edoxaban demonstrated non-inferiority for stroke or SE.[12] Edoxaban was also found to be superior for the principal safety endpoint of major bleeding in comparison to warfarin.[12]

Appropriate Use of Edoxaban.

Haemorrhage is a common adverse effect of all anticoagulants.

- Special care should be taken when deciding to prescribe edoxaban to patients with other conditions, procedures, and concomitant treatments, which may increase the risk of major bleeding.
- As such, a detailed prescriber guide has been made available to HCPs to ensure correct use of the drug
- In addition, every pack contains a patient alert card which can help alert treating HCPs in the case of routine or emergency interventions

The prescriber guide and a full list of contraindications, warnings and information on posology can be found in the edoxaban summary of product characteristics at https://www.medicines.org.uk/emc/medicine/30506

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.

Contact

Lydia Worms (Europe)
Daiichi Sankyo Europe GmbH
Edoxaban Communications & Product PR Europe
+49 (89) 7808751

Yasuki Minobe (Global)
Daiichi Sankyo Group
Corporate Communications Department
+81 (3) 62251126

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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