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Press Release

Daiichi-Sankyo

UK's NICE recommends once-daily LIXIANA® (edoxaban) for the treatment and prevention of recurrent deep vein thrombosis and pulmonary embolism in adults

Tokyo, Japan (August 26, 2015) - The National Institute for Health and Care Excellence (NICE), the medicines cost-effectiveness body for England and Wales, has today recommended a new treatment to help patients suffering from blood clots in the legs and lungs.[1]

Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) today announced that NICE has issued its final recommendation for LIXIANA® (edoxaban) for the treatment and prevention of recurrent deep vein thrombosis (DVT) and pulmonary embolism (PE) in adults.

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

- Treatment of DVT and PE, and prevention of recurrent DVT and PE in adults
- Prevention of stroke and systemic embolism (SE) in adult patients with nonvalvular atrial fibrillation (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)

The final NICE recommendation states: "Edoxaban is recommended, within its marketing authorisation, as an option for treating and for preventing recurrent deep vein thrombosis and pulmonary embolism in adults."[1] It adds: "The Committee concluded that edoxaban could be recommended as a cost-effective use of National Health Service (NHS) resources."[1]

On August 6, 2015, NICE also published a Final Appraisal Determination (FAD) for its Single Technology Appraisal (STA) of LIXIANA® for the prevention of stroke and SE in people with NVAF.[2]

Edoxaban, invented by the pharmaceutical company Daiichi Sankyo, is a member of the class of blood-thinning drugs known as novel oral anticoagulants (NOACs). The 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 or drug interactions.

Once daily edoxaban is initiated after a five day lead in with heparin treatment, in line with current clinical practice. In the pivotal Hokusai-VTE study, edoxaban was shown to have proven efficacy and a significantly better bleeding profile than well-managed warfarin.[3]

The term venous thromboembolism (VTE) is used to cover both DVT and PE. VTE is associated with considerable clinical burden related to recurrence and complications including post-thrombotic syndrome and pulmonary hypertension, and is often fatal. The number of casualties in Europe annually due to VTE is double that of people who die of breast cancer, prostate cancer, AIDS and traffic accidents combined.[4]

There is a high rate of recurrence after a first VTE event, which is reduced with anticoagulant treatment. Without anticoagulant treatment, approximately half of patients who experience an initial VTE event have recurrent VTE within three months.[5]

According to NICE, there are approximately 83,500 new cases of VTE each year in England. This equates to approximately one case per 500 people (200 cases per 100,000).[6] In addition to new annual cases, there is another group of approximately 42,000 patients needing long-term anticoagulation treatment.[6]

A 2007 study of morbidity and mortality from VTE in six European countries (France, Germany, Italy, Spain, Sweden and the UK) estimated a total of approximately 762,000 VTE episodes and a further 370,000 VTE-related deaths each year. Of these deaths, almost 60% followed undiagnosed and untreated VTE, which suggests that effective treatment could prevent many VTE-related deaths.[4]

Dr Alexander Cohen, Consultant Vascular Physician from Guy's and St Thomas' Hospitals, Kings College London, who has researched edoxaban for VTE, welcomed an additional resource to tackle the condition.

"No two patients are identical and what suits one may not suit another. Venous thromboembolism has a high rate of recurrence, which can be fatal. We need more tools to protect patients from a second incident and edoxaban will be of great use to doctors to help tailor treatments to specific patients."

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 and convenient-to-use alternative in the treatment armoury against VTE. It is gratifying that NICE has found our therapy to be clinically effective and cost effective shortly after receiving our European authorisation."

About VTE

VTE is a condition in which a blood clot (a thrombus) forms in a vein, most commonly in the deep veins of the legs or pelvis. This is known as DVT.[7] The thrombus can dislodge and travel in the blood (an embolus), particularly to the pulmonary (lung) arteries. This is known as PE. The term VTE includes both DVT and PE.[7] Venous thromboembolic diseases cover a spectrum ranging from asymptomatic calf vein thrombosis to symptomatic DVT. They can be fatal if they lead to PE, in which the blood supply to the lungs is blocked by the thrombus. Non-fatal VTE can cause serious long-term conditions such as post-thrombotic syndrome.[7]

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.

The global phase 3 Hokusai-VTE study investigated 8,292 patients with either acute symptomatic DVT, PE, or both. This represented the largest single VTE study carried out to date with a NOAC in this indication.[3]

The study found that edoxaban met the primary efficacy endpoint of non-inferiority compared to warfarin, following initial use of heparin in both arms, for the treatment and prevention of recurrent symptomatic VTE.[3]

Once-daily edoxaban also demonstrated superiority compared to warfarin for the principal safety outcome of clinically relevant bleeding (the composite of major or clinically relevant non-major bleeding).[3]

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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.

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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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