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News release for national newspapers, patient groups, medical, pharmacy and pharmaceutical trade media

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NICE recommends Xarelto® (rivaroxaban) use in NHS

Without preventative treatment, 45,000 people undergoing elective hip or knee replacement every year in England could develop a potentially fatal blood clot. NICE now recommends Xarelto® – a new, oral anticoagulant, up to 70% more effective at reducing blood clots than the current gold standard (injectable enoxaparin).

London, 22nd April 2009 – The National Institute for Health and Clinical Excellence (NICE) has today recommended the new oral anticoagulant Xarelto® (rivaroxaban), within its licensed indication, as a treatment option for the prevention of potentially fatal blood clots (venous thromboembolism) in adults undergoing elective hip or knee replacement surgery. After a large scale clinical trial programme involving over 12,500 patients, Xarelto® has a wealth of evidence supporting its clinical and cost-effectiveness and has received this positive appraisal from NICE within seven months of its launch in the UK.[1]

Until recently, anticoagulant therapy often required administration by injection and little had advanced in terms of new treatments for over fifty years.[2] Two new oral anticoagulants came to market during 2008, each working in a different way. Xarelto® – an oral direct Factor Xa inhibitor – is the first of a new generation of oral anticoagulants and the first to demonstrate superior efficacy to the current standard of care, injectable enoxaparin, whilst maintaining a comparable side-effect profile.[3,4]

Venous thromboembolism (VTE) is a leading cause of preventable hospital deaths in the UK, causing 10 per cent of all deaths from hospital stays – up to 32,000 people each year – more than HIV/AIDS, breast cancer, and road traffic accidents combined.[5] Major orthopaedic surgery is associated with a particularly high risk of hospital-acquired VTE – more than half of the 90,434 people undergoing elective hip or knee replacement every year in England[6]

could develop a potentially fatal blood clot if no preventative treatment (known as thromboprophylaxis) is given.[7]

Professor Beverley Hunt, Consultant Haematologist and Medical Director of Lifeblood: The Thrombosis Charity, welcomes NICE's positive decision: "It is terrific that NICE has approved Xarelto® so quickly. A new highly effective oral anticoagulant will encourage thromboprophylaxis implementation and greatly reduce the risk of hospital-acquired clots after planned major orthopaedic surgery."

In a large-scale Phase III clinical trial programme involving over 12,500 patients, rivaroxaban became the first oral anticoagulant to demonstrate superior efficacy over the current standard of care (injected enoxaparin). In these trials, rivaroxaban reduced the combined total of VTEs and deaths by between 49–70%.[3,4,8] In addition to these efficacy advantages, rivaroxaban has other benefits compared with currently available treatment options because it is given as a one tablet, once-daily, fixed-dose regimen that eliminates the need for any routine monitoring (such as coagulation (clotting), liver function etc) or dose adjustment.[9]

Professor Ajay Kakkar, Professor of Surgical Sciences at the Barts and the London School of Medicine and Dentistry, and Director of the Thrombosis Research Institute, London said, "NICE's recommendation about rivaroxaban is very positive. Venous thromboembolism is the commonest avoidable cause of hospital death. Today's announcement means we have another effective method to prevent potentially fatal blood clots in orthopaedic surgical patients. In particular we can now facilitate the use of preventative methods out of hospital."

VTE costs the NHS an estimated £640 million per year.[5] A further £19 million of NHS money is spent on litigation from patients who have developed blood clots as a result of a hospital stay or procedure.[10]

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NOTES FOR EDITORS

National Institute for Health and Clinical Excellence recommendation*:

> **Rivaroxaban (Xarelto®),** within its marketing authorisation, is recommended as an option for the prevention of venous thromboembolism in adults having elective total hip replacement surgery or elective total knee replacement surgery.

http://www.nice.org.uk/guidance/index.jsp?action=download&o=43417

About hospital-acquired DVT

- Venous blood clots, (also known as venous thromboembolism or VTE) can take the form of either:
    - A deep vein thrombosis (DVT) - a blood clot in a deep vein (usually in the leg) that partially or totally blocks the flow of blood[11]
    - A pulmonary embolism (PE) - a blood clot blocking an artery in the lungs[11]
- Each year up to 32,000 people in the UK die from venous blood clots as a result of a hospital stay or surgical procedure (sometimes referred to as 'hospital-acquired DVT'). This is more people than die from breast cancer, HIV/AIDS and road traffic accidents combined[5]
- Many of these deaths could be prevented[5]
- Effective prevention and treatment of hospital-acquired DVT is a major national public health issue[5]
- People at risk of hospital-acquired DVT include people undergoing major orthopaedic surgery and those who are hospitalised or immobilised over long periods [12,13]
- The majority (74%) of hospital-acquired DVT cause symptoms after the patient has left hospital[13]
- Hospital-acquired DVT occur in up to 50% of patients undergoing major orthopaedic surgery who do not receive preventative care[7]
- In November 2008, the All-Party Parliamentary Thrombosis Group (APPTG) published their second annual report which showed that 70% of acute hospital trusts are now taking steps to risk assess patients for hospital-acquired DVT[14] – compared with only 32% in their 2007 report.[15] These findings demonstrate that more hospitals are now bringing their practices in line with NICE and government recommendations, which are as follows:
    - Current NICE recommendations state that:[16]
        - All patients undergoing major surgery should be assessed to identify their individual risk of developing VTE after the procedure

        - All patients undergoing major orthopaedic surgery of the lower limbs should receive anticoagulant therapy, LMWH (low molecular weight heparin) for up to 28 days after surgery in combination with pressure stockings, to reduce the risk of VTE
    - SIGN guidelines recommend patients undergoing total hip or knee replacement surgery should be considered for both pharmaceutical thromboprophylaxis for up to five weeks following surgery, and mechanical methods of thromboprophylaxis[17]

About Xarelto® (rivaroxaban)

Xarelto® is licensed for the prevention of venous thromboembolism in adult patients undergoing elective hip or knee replacement surgery. It is the first of a new class of oral anticoagulant specifically inhibiting Factor Xa, a pivotal step in the coagulation (blood clotting) process.[18]

Unlike low molecular weight heparins, such as enoxaparin, which are administered daily by injection, Xarelto® is an oral, one tablet once-daily treatment which is administered six to ten hours after surgery.[19] It is licensed for two weeks following elective knee replacement surgery or five weeks following elective hip replacement surgery. An oral tablet such as Xarelto® offers a more convenient, patient orientated treatment option than an injection as it enables patients to more easily continue their anticoagulant therapy at home, providing ongoing protection against the continued risk of developing clots. Further, there are no routine coagulation monitoring requirements with Xarelto®.

More than 60,000 patients are expected to be enrolled into the Xarelto clinical development program, which will evaluate the product in the prevention and treatment of a broad range of acute and chronic blood-clotting disorders.

About Bayer Schering Pharma UK

Bayer Schering Pharma is a leading, worldwide speciality pharmaceutical company. Its research and business activities are focussed on the fields of haematology & cardiology, oncology, diagnostic imaging, primary care, specialised therapeutics and women's healthcare. With innovative products and using new ideas, Bayer Schering Pharma aims to make a contribution to medical progress and strives to improve the quality of life of patients.

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Forward-Looking Statements

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