



News release for medical media

Venous Blood Clot Prevention after Elective Hip or Knee Replacement Surgery:

Bayer's Novel Anticoagulant Rivaroxaban Recommended for Approval in the EU

Final approval from the European Commission expected within the next few months

July 25, 2008 – The European Committee for Medicinal Products for Human Use (CHMP) has recommended approval of the anticoagulant rivaroxaban (Xarelto®), taken as one tablet, once-daily, for the prevention of venous blood clots (deep vein thrombosis (DVT) and pulmonary embolism (PE)) in patients undergoing elective (planned) hip or knee replacement surgery. It is expected that final approval by the European Commission will follow in the next few months, providing marketing authorisation for rivaroxaban in all EU member states.

The recommendation for approval of rivaroxaban, which comes just nine months after its submission, is based on review of the extensive RECORD clinical trial programme in which rivaroxaban, an oral, direct Factor Xa inhibitor, demonstrated its significant clinical potential when compared to the current standard of care, enoxaparin, an injectable low molecular weight heparin (LMWH).

The limitations of current treatment mean that many patients still do not receive satisfactory anticoagulant therapy to prevent potentially fatal clots. “The prevention and treatment of thrombosis remains a challenge for patients requiring chronic therapy. The availability of agents such as rivaroxaban has the potential for a substantial impact on patient care.” Said Professor Ajay Kakkar, Professor of

Surgical Sciences at Barts and the London School of Medicine and a Principal Investigator in the RECORD programme.

Involving nearly 10,000 patients undergoing elective hip or knee replacement surgery, the Phase III RECORD trials demonstrated superior efficacy of rivaroxaban in both head-to-head comparisons with enoxaparin (RECORD 1&3)^{1,2} and when comparing extended-duration (x five weeks) rivaroxaban with short duration (x two weeks) enoxaparin (RECORD2).³ In all three trials, rivaroxaban and enoxaparin had comparable safety profiles and similar low rates of bleeding.

Commenting on the CHMP recommendation, Beverley Hunt, Medical Director, Lifeblood: The Thrombosis Charity; "Hospital-acquired DVT is a major patient safety issue. A treatment which improves upon our current standard of care as well as making extended thromboprophylaxis more accessible is an extremely important advance."

The extensive clinical trial programme supporting rivaroxaban makes it the most studied oral direct Factor Xa inhibitor in the world today. Almost 50,000 patients are expected to be enrolled overall into the rivaroxaban clinical development programme which will evaluate the product in the prevention and treatment of a broad range of acute and chronic blood-clotting disorders such as venous thromboembolism (VTE) treatment, stroke prevention in patients with atrial fibrillation, VTE prevention in hospitalised, medically ill patients and secondary prevention of acute coronary syndrome.

Bayer estimates the global peak sales potential of rivaroxaban for all indications to exceed EUR 2 billion.

-Ends-

CONTACT FOR FURTHER INFORMATION:

Athena Medical PR

Emma Keeling

Tel: 020 8956 2299

Mobile: 07884 311982

emmak@athenamedicalpr.com

Natalie Bennett

Tel: 020 8956 2299

Mobile: 07786 078745

natalie@athenamedicalpr.com

NOTES FOR EDITORS

About VTE

- Venous thromboembolism (VTE) is a term which encompasses two conditions:
 - Deep vein thrombosis (DVT) – a blood clot in a deep vein (usually the leg) which partly or totally blocks the flow of blood
 - Pulmonary embolism (PE) – an often fatal condition which occurs when part of the blood clot travels to and blocks the arteries in the lungs
- 10% of hospital deaths are caused by VTE, making it the leading cause of hospital deaths⁴
- VTE kills up to 60,000 people each year in the UK, a figure that is five times greater than the combined total number of deaths from breast cancer, AIDS, and road traffic incidents⁴
- Patients undergoing major orthopaedic surgery, such as hip or knee replacement are at high risk of VTE due to the combination of immobility and surgical trauma
- In November 2007, the All Party Parliamentary Thrombosis Group (APPTG) published a report following an audit of acute hospital trusts which found that only 32% of hospital trusts are taking steps to risk assess patients (for VTE) and bring their practices in line with NICE and government recommendations⁵ which are as follows:
 - Current NICE recommendations state that:⁶
 - 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

About Rivaroxaban

Rivaroxaban is a novel, oral, once-daily direct Factor Xa inhibitor in advanced clinical development for a wide range of indications to prevent and treat blood clots. Rivaroxaban works at a pivotal stage in the coagulation pathway to directly inhibit the enzyme Factor Xa.

To date, rivaroxaban is the most studied oral, direct Factor Xa inhibitor in development. More than 20,000 patients have been evaluated in the completed Phase II programmes and enrolled thus far in the Phase III programmes. Almost 50,000 patients are expected to be evaluated in total.

Bayer HealthCare submitted a regulatory filing to the European Agency for the Evaluation of Medicinal Products (EMA) at the end of October 2007 for approval to market rivaroxaban in the EU for the prevention of VTE in patients undergoing major orthopaedic surgery of the lower limbs.

The trade name of rivaroxaban is expected to be Xarelto[®], pending health authority approval.

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.

References

1. Eriksson BI, Borris LC, Friedman RJ et al. Rivaroxaban versus enoxaparin for thromboprophylaxis after hip arthroplasty. *N Engl J Med* 2008;358:-2765-75
2. Lassen MR, Ageno W, Borris LC et al. Rivaroxaban versus enoxaparin after total knee arthroplasty. *N Engl J Med* 2008; 358:2776 - 86
3. Kakkar AK, Brenner B, Dahl OE et al. Extended duration rivaroxaban versus short-term enoxaparin for the prevention of venous thromboembolism after total hip arthroplasty: a double-blind, randomised controlled trial. *The Lancet* 2008; 372:29-37
4. Fitzmaurice DA. Thromboprophylaxis for adults in hospital. *BMJ* 2007; 334: 1017-8
5. All-Party Parliamentary Thrombosis Group (APPTG) VTE Research Report, April 19 2007
6. NICE Clinical Guideline 46. Venous Thromboembolism: Reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in in-patients undergoing surgery. April 2007