# NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

## Health Technology Appraisal

## Rivaroxaban for the prevention of venous thromboembolism after elective orthopaedic surgery of the lower limbs

## Final scope

### Remit/appraisal objective

To appraise the clinical and cost effectiveness of rivaroxaban within its licensed indication for the prevention of venous thromboembolism after elective orthopaedic surgery of the lower limbs

### Background

Venous thromboembolism (VTE) is the blocking of a blood vessel by a blood clot either in situ or one that has dislodged from its site of origin and travelled around the circulation to block other vessels. VTE includes deep vein thrombosis (DVT) with clots in the deep veins in the legs, thighs or pelvis; and pulmonary embolism (PE) with dislodged clots blocking the pulmonary vessels in the lungs. DVT is associated with inactivity and major procedures involving orthopaedic surgery and lengthy operations.

DVT is often asymptomatic, but patients may experience swelling and pain in the legs. Thrombi can also cause long-term symptoms such as chronic leg pain, swelling, dermatitis and ulcers and this is referred to as post-thrombotic syndrome. Symptoms of PE include breathlessness, haemoptysis and chest pain. Large pulmonary emboli can cause sudden death due to heart failure. Those surviving a large PE often require intensive care, and recovery can take several weeks or months.

There were 59,205 hip replacement operations and 56,652 knee replacement operations in England in a 12 month period 2004/5. Without anticoagulant prophylaxis the incidence of nonfatal clinical DVT with PE is up to 5% in hip replacement, up to 14% in knee replacement. The overall risk of fatal PE following high risk surgery has been estimated to be between 0.2 and 0.3%.

The NICE clinical guideline on the prevention of venous thromboembolism in patients undergoing orthopaedic surgery and other high-risk surgical procedures (CG 046) recommends mechanical prophylaxis (such as graduated elastic compression stockings and intermittent pneumatic compression devices and mechanical foot pumps). In addition to mechanical prophylaxis, patients at increased risk of venous thromboembolism (VTE) should be offered low molecular weight heparin (LMWH). Fondaparinux, within its licensed indications, may be used as an alternative to LMWH. Patients having hip replacement surgery with one or more risk factors should have their LMWH or fondaparinux continued for four weeks after surgery.

## The technology

Rivaroxaban (Xarelto, Bayer HealthCare) is an anticoagulant which acts by direct inhibition of activated factor X (factor Xa). Factor Xa is a key component in the formation of blood clots.

Rivaroxaban received positive opinion from the Committee for Medicinal Products for Human use (CHMP) on 24 July 2008 and is likely to be indicated for prevention of venous thromboembolism (VTE) in adult patients undergoing elective hip or knee replacement surgery. Rivaroxaban does not currently hold a UK marketing authorisation.

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| **Intervention(s)** | Rivaroxaban |
| **Population(s)** | Adults undergoing elective hip or knee replacement surgery |
| **Standard comparators** | Pharmacological methods of prophylaxis using one of the following drugs:<br>• low-molecular-weight heparin<br>• fondaparinux<br>• dabigatran |
| **Outcomes** | The outcome measures to be considered include:<br>• mortality<br>• incidence of DVT/PE<br>• post DVT complications including post thrombotic syndrome<br>• length of hospital stay<br>• health-related quality of life.<br>• adverse effects of treatment including bleeding events (minor and major/clinically relevant bleeding)<br>• joint outcomes (medium and long-term), including joint infection. |

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| **Economic analysis** | The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.<br><br>The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.<br><br>Costs will be considered from an NHS and Personal Social Services perspective. |
| **Other considerations** | The duration of treatment with rivaroxaban in RCTs has been longer for patients undergoing elective hip surgery compared with those undergoing knee surgery. This, and other factors affecting clinical and cost effectiveness, would indicate that separate analysis for different types of surgery is necessary.<br><br>There may also be subgroups of patients who can be identified as being at higher or lower risk of DVT and/or PE, for example as a result of co-morbidities.<br><br>Guidance will only be issued in accordance with the marketing authorisation. |
| **Related NICE recommendations** | Related Technology Appraisals:<br><br>Technology Appraisal in Preparation: 'Dabigatran etexilate for the prevention of venous thromboembolism after hip or knee replacement surgery in adults' Earliest anticipated date of publication to be confirmed.<br><br>Related Guidelines:<br><br>NICE Clinical Guideline No. 46 - 'Venous thromboembolism - the prevention of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in patients undergoing orthopaedic surgery and other high-risk surgical procedures', April 2007.<br><br>The prevention of venous thromboembolism in all hospital patients. NICE Clinical Guideline, in progress. |