NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Apixaban for the prevention of venous thromboembolism in people undergoing elective knee and hip replacement surgery

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of apixaban, within its licensed indication, for the prevention of venous thromboembolism in people undergoing elective knee and hip replacement surgery.

Background

Venous thromboembolism (VTE) is a term used to describe deep vein thrombosis and pulmonary embolism. DVT is the formation of a thrombus in a deep vein, usually of the lower limbs. Distal DVTs are those in deep veins of the calf, and are the most common type of DVT. Proximal DVTs are those that extend to the popliteal, superficial femoral, common femoral, or iliac veins. With DVT, dislodged thrombi may travel to the lungs and this is called pulmonary embolism (PE). Massive PE can cause sudden death and those who survive a PE often require intensive care and recovery can take several weeks or months.

The incidence of VTE in the general population is estimated to be 1 in 2000 in the UK. There are a number of risk factors for VTE, which include cancer, increasing age, obesity, and inherited or acquired clotting tendency. In addition, inactivity and high-risk surgical procedures can lead to VTE and the risk is particularly high in patients undergoing orthopaedic surgery and lengthy operations. Without anticoagulant prophylaxis, the estimated incidence of DVT ranges from 27% after elective knee surgery to 44% after elective hip surgery. The incidence of nonfatal clinical DVT with PE is up to 5% in hip replacement and 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 VTE in patients undergoing orthopaedic surgery and other high-risk surgical procedures (CG46) recommends mechanical and physical prophylaxis. This includes early mobilisation and leg exercises, compression stockings and devices and mechanical foot pumps. In addition to mechanical prophylaxis, patients at increased risk of VTE should be offered low molecular weight heparin (LMWH), such as enoxaparin. Fondaparinux, within its licensed indications, may be used as an alternative to LMWH. NICE technology appraisal TA157 recommends dabigatran etexilate as a treatment option for the prevention of VTE in patients having elective total knee or hip replacement surgery. NICE technology appraisal TA170 recommends rivaroxaban as a treatment option

for the prevention of VTE in patients having elective knee or hip replacement surgery.

The technology

Apixaban (brand name to be confirmed, Bristol Myers Squibb and Pfizer) is a direct oral factor Xa inhibitor which prevents the formation of thrombin and fibrin; the key components in blood clot formation.

Apixaban does not have a UK marketing authorisation for the prevention of VTE events in people undergoing elective knee or hip surgery. It has been studied in clinical trials compared with enoxaparin for the prevention of VTE in people undergoing elective knee replacement surgery, and is being studied in comparison with enoxaparin in people undergoing elective hip replacement surgery.

Intervention(s)	Apixaban
Population(s)	People undergoing elective knee or hip replacement surgery
Comparators	Pharmacological methods of prophylaxis using one of the following drugs: • low molecular weight heparin • fondaparinux • rivaroxaban • dabigatran etexilate
Outcomes	The outcome measures to be considered include: • mortality • incidence of VTE • post DVT complications including thrombotic syndrome • length of hospital stay • joint outcomes (medium and long term), including joint infection • adverse effects of treatment including bleeding events • health-related quality of life

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. 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. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No 157, September 2008. Dabigatran etexilate for the prevention of venous thromboembolism after hip or knee replacement surgery in adults. Review date June 2011. Technology Appraisal No 170, April 2009. Rivaroxaban for the prevention of venous thromboembolism after total hip or total knee replacement in adults. Review date February 2012. Related Guidelines: Clinical Guideline No 46, April 2007. Venous thromboembolism: reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in patients undergoing surgery. Clinical Guideline (in progress, earliest anticipated publication date November 2009). Reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in patients admitted to hospital.

Questions for consultation

Have the most appropriate comparators for the prevention of VTE in people who are undergoing elective hip or knee replacement surgery been included in the scope? Are the comparators listed routinely used in clinical practice?

Are there any subgroups of patients in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Are there factors affecting patient management or clinical and cost effectiveness, that would indicate that separate analysis for different types of surgery is necessary?

Are there any issues that require special attention in light of the duty to have due regard to the need to eliminate unlawful discrimination and promote equality?

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)