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

Final scope

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 occasionally require intensive care and recovery can take several weeks or months. DVT can also cause long-term morbidity due to the development of post-thrombotic syndrome, (chronic leg pain, swelling, dermatitis and ulcers resulting from the destruction of leg vein valves).

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, for example heart failure, 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 prevalence of DVT ranges from 41 to 85% after elective knee surgery to 42 to 57% after elective hip surgery. The prevalence of DVT with PE is up to 0.9 to 28% in hip replacement and up to 1.5 to 10% 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 reducing the risk of VTE in patients admitted to hospital (CG92) recommends combined prophylaxis with mechanical and pharmacological methods for patients undergoing elective knee and hip replacement surgery. Mechanical prophylaxis includes the use of one of compression stockings, foot impulse devices, and intermittent pneumatic compression devices, continued until the patient no longer has significantly reduced mobility. In addition to mechanical prophylaxis, patients should be offered one of dabigatran etexilate (starting 1 to 4 hours after surgery), fondaparinux sodium (starting 6 hours after surgical closure provided

haemostasis has been established), low molecular weight heparin (LMWH) (starting 6–12 hours after surgery), rivaroxaban (starting 6–10 hours after surgery), and unfractionated heparin for patients with renal failure (starting 6–12 hours after surgery). Pharmacological VTE prophylaxis should be continued for 28 to 35 days in patients undergoing hip replacement or 10 to14 days in patients undergoing knee replacement. Dabigatran etexilate and rivaroxaban are recommended in CG92 in line with their respective NICE technology appraisal guidance TA157 and TA170.

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 and 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 (symptomatic and asymptomatic) • 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 Hips surgery and knee surgery should be analysed as separate subgroups

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 92, January 2010. Reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in patients admitted to hospital.