NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Dabigatran etexilate for the prevention of venous thromboembolism after hip or knee replacement surgery in adults

Final Scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of dabigatran etexilate within its licensed indication for the prevention of venous thromboembolism after elective hip or knee replacement surgery in adults.

Background

Venous thromboembolism 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. DVT is associated with inactivity and high-risk surgical procedures and the risk is particularly high in patients undergoing orthopaedic surgery and lengthy operations.

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.

Undergoing orthopaedic surgery significantly increases the risk of DVT, which (if DVT occurs) can 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).

In a 12 month period 2004/5 in England, there were 56,652 knee replacement operations and 59,205 hip replacement operations. 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

pulmonary embolism 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.

The technology

Dabigatran etexilate (Pradaxa, Boehringer Ingelheim Ltd) is an oral direct thrombin inhibitor given post-operatively that specifically and reversibly inhibits thrombin, an enzyme involved in blood clot formation. Dabigatran etexilate does not currently hold a UK marketing authorisation. The clinical trials for dabigatran etexilate for the prevention of venous thromboembolism included patients undergoing elective total hip or total knee replacement surgery.

Intervention(s)	Dabigatran etexilate
Population(s)	Adults undergoing elective hip or knee replacement surgery.
Standard comparators	Pharmacological methods of prophylaxis using one of the following drugs: • low-molecular-weight heparin • fondaparinux

Outcomes	The outcome measures to be considered include: • mortality • incidence of DVT • incidence of PE • post DVT complications including post thrombotic syndrome • length of hospital stay • health-related quality of life. • adverse effects of treatment including bleeding events (minor and major) • joint outcomes (medium and long-term), including joint infection.
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 time horizon for the economic evaluation should be appropriate for the nature of the condition. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	The duration of treatment with dabigatran etexilate is different for patients undergoing elective hip or knee surgery. Therefore the analysis of cost effectiveness will have to be done separately for the two conditions. There may also be subgroups of patients who can be identified as being at higher or lower risk of DVT, for example as a result of co-morbidities. Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations	Related Guidelines: 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. The prevention of venous thromboembolism in all hospital patients**.** NICE Clinical Guideline, in progress.