NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Rivaroxaban for the prevention of venous thromboembolism in people hospitalised for acute medical conditions

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of rivaroxaban within its licensed indication for the prevention of venous thromoboembolism in people hospitalised for acute medical conditions.

Background

Venous thromboembolism is a condition in which a blood clot (thrombus) forms in a vein. It most commonly occurs in deep veins in the legs or pelvis which is called deep vein thrombosis. Blood clots can become dislodged from the site of origin and travel in the blood. If a blood clot blocks a blood vessel, this is called an embolism. If the blood flow is blocked from the heart to the lungs, this is called pulmonary embolism. Pulmonary embolism can be fatal. People who survive a pulmonary embolism occasionally require intensive care and recovery can take several weeks or months. Other complications of deep vein thrombosis include post thrombotic syndrome, where blood pools in a person's leg causing long-term pain, swelling, and in severe cases, ulcers; and also limb ischaemia, a rare complication where the blood clot restricts the flow of oxygen to the affected leg and may cause skin ulcers, infection and gangrene.

Venous thromboembolism has an annual incidence of approximately 1 in 2000 of the general population in the UK. This rate varies substantially with age. There are numerous risk factors for venous thromboembolism, which include active cancer or cancer treatment, age over 60 years, critical care admission, dehydration, known tendency to develop blood clots, obesity, the presence of comorbidities such as heart disease and metabolic pathologies, family history, use of hormone replacement therapy or oestrogen-containing contraceptive therapy and varicose veins with phlebitis. In addition, venous thromboembolism can occur during acute medical illness, which may include myocardial infarction, stroke, spinal cord injury and severe infection or exacerbation of chronic obstructive pulmonary disease.

Venous thromboembolism is most often associated with surgery, however 70-80% of hospital-acquired fatal pulmonary embolism occurs in patients who are not undergoing surgery. About 40% of patients hospitalised for medical conditions have more than one risk factor for venous thromboembolism. The baseline risk of venous thromboembolism is estimated to be around 15% for those who are acutely unwell in medical beds, with risks rising to about 50-60% if the person has had a severe stroke. It is estimated that 25,000 people

in the UK die from preventable hospital-acquired venous thromboembolism every year.

In clinical practice, pharmacological prevention is given to people with acute medical conditions who are at risk of developing venous thromboembolism. This is usually given until the perceived risk is reduced to the extent that preventative treatment is not required. NICE clinical guideline 92 (CG92) recommends fondaparinux sodium, low molecular weight heparin (such as enoxaparin) and unfractionated heparin (for people with renal failure).

The technology

Rivaroxaban (Xarelto, Bayer) 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. It is administered orally.

Rivaroxaban does not hold a UK marketing authorisation for the prevention of venous thromboembolism in people hospitalised for acute medical conditions. It is being studied in a clinical trial compared with enoxaparin for the prevention of venous thromboembolism in adults (aged 40 years or over) hospitalised for acute medical conditions including heart failure, acute ischemic stroke, acute infectious and inflammatory diseases including acute rheumatic diseases, acute respiratory insufficiency and active cancer.

Intervention(s)	Rivaroxaban
Population(s)	People who are hospitalised for acute medical conditions and are at risk of venous thromboembolism
Comparators	• low molecular weight heparin • fondaparinux sodium
Outcomes	The outcome measures to be considered include: • mortality • incidence of deep vein thrombosis • incidence of pulmonary embolism • complications following deep vein thrombosis, including post thrombotic syndrome • length of hospital stay • 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. If evidence allows, subgroups will be considered by differential baseline risk of venous thromboembolism. If evidence allows, the analysis should consider a distinction between symptomatic and asymptomatic venous thromboembolism.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal in preparation, Apixaban for the prevention of venous thromoboembolism in acute medical illness. Expected date of publication TBC. 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. Review date TBC. Clinical guideline in preparation, Management of venous thromboembolic diseases. Expected date of publication June 2012.

Questions for consultation

Have the most appropriate comparators for rivaroxaban for the treatment of venous thromobembolism been included in the scope? Are the comparators listed routinely used in clinical practice?

- Which types of low molecular weight heparin are routinely used in clinical practice?

Are the subgroups suggested in ‘other considerations appropriate? Are there any other subgroups of people in whom rivaroxaban is expected to be more clinically effective and cost effective or other groups that should be examined separately?

- How is baseline risk of venous thromboembolism assessed in clinical practice?

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?

Do you consider rivaroxaban to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of rivaroxaban can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

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)