NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Dabigatran etexilate for the treatment and secondary prevention of symptomatic venous thromboembolism

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of dabigatran etexilate within its licensed indication for the treatment and secondary prevention of symptomatic venous thromboembolism.

Background

Venous thromboembolism is a term used to describe deep vein thrombosis and pulmonary embolism. Deep vein thrombosis is the formation of a thrombus in a deep vein, usually of the lower limbs. With deep vein thrombosis, dislodged thrombi may travel to the lungs and this is called pulmonary embolism. Pulmonary embolism can cause sudden death and those 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, a chronic disorder that may include symptoms such as pain, heaviness, swelling, cramps, itching or tingling, increased skin pigmentation and ulceration in the affected limb. In addition, chronic thromboembolic pulmonary hypertension is a rare but potentially treatable cause of pulmonary hypertension.

Venous thromboembolism has an annual incidence of approximately 1 in 2000 of the general population in the UK. This rate varies substantially with age - for people under 40 years the annual incidence of venous thromboembolism is 1 in 10,000, whereas for people over 80 years the incidence rises to 1 in 100. People who have had an episode of venous thromboembolism have a risk of recurrence within 8 years of approximately 30%. However, the risk of recurrence decreases substantially with time and may vary according to the treatment received.

NICE clinical guideline 144 states that patients with confirmed proximal deep vein thrombosis or pulmonary embolism should be offered a choice of low molecular weight heparin or fondaparinux (or unfractionated heparin for those with severe renal impairment, established renal failure or people with pulmonary embolism and haemodynamic instability). The vitamin K antagonist warfarin can be offered to patients with confirmed proximal deep vein thrombosis or pulmonary embolism within 24 hours of diagnosis and continued for 3 months or beyond depending on their risk of bleeding. For people in whom a vitamin K antagonist is not considered an appropriate treatment, unfractionated heparin or low molecular weight heparin may be

continued instead of a vitamin K antagonist. Some people may require long term treatment to prevent recurrence. Frequent monitoring and possible adjustment of dose is required with the use of vitamin K antagonists.

NICE Technology Appraisal 261 recommends rivaroxaban as an option for treatment and prevention of deep vein thrombosis.

The technology

Dabigatran etexilate (Pradaxa, Boehringer Ingelheim) is a direct thrombin inhibitor that specifically and reversibly inhibits thrombin, a key enzyme in blood clot formation. It is administered orally.

Dabigatran etexilate does not currently hold a UK marketing authorisation for the treatment and secondary prevention of venous thromboembolism. It has been studied in a clinical trial of adults with acute symptomatic venous thromboembolism in comparison with warfarin. It has also been compared with placebo in a clinical trial of adults with symptomatic deep vein thrombosis or pulmonary embolism who have completed 6 to 18 months of treatment with a vitamin K antagonist.

Dabigatran etexilate holds a UK marketing authorisation for the primary prevention of venous thromboembolism in adults who have undergone elective total hip or total knee replacement surgery.

Intervention(s)	Dabigatran etexilate
Population(s)	People with symptomatic venous thromboembolism (deep vein thrombosis or pulmonary embolism)
Comparators	• Initial treatment with a low molecular weight heparin (such as enoxaparin) with continued therapy as follows: - vitamin K antagonists (such as warfarin) • Fondaparinux • Rivaroxaban

Outcomes	The outcome measures to be considered include: • mortality • venous thromboembolism recurrence • complications following deep vein thrombosis or pulmonary embolism, including post thrombotic syndrome, chronic thromboembolic pulmonary hypertension and heart failure. • adverse effects of treatment (including clinically relevant bleeding) • 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 261, July 2012. Rivaroxaban for the treatment and secondary prevention of venous thromboembolism. Review decision date May 2015. 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. Clinical guideline No 144, June 2012. Management of venous thromboembolic diseases. Related Interventional Procedures: Interventional Procedure No 349, June 2010. Percutaneous occlusion of the left atrial appendage in non-valvular atrial fibrillation for the prevention of thromboembolism. Related Pathways:

	Venous thromboembolism, May 2011 Related Quality Standards: VTE prevention quality standard, June 2010

Questions for consultation

Have the most appropriate comparators for dabigatran etexilate for the treatment and secondary prevention of symptomatic venous thromboembolism been included in the scope?

- Are the comparators listed routinely used in clinical practice?

Are there any subgroups of people in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately? In particular, should people with deep vein thrombosis and pulmonary embolism be considered separately?

What do you consider to be the relevant clinical outcomes and other potential health related benefits of dabigatran etexilate for the treatment and secondary prevention of symptomatic venous thromboembolism particularly when compared with currently used treatment options?

Please consider whether in the remit or the scope there are any issues relevant to equality. Please pay particular attention to whether changes need to be made to the remit or scope in order to promote equality, eliminate unlawful discrimination, or foster good relations between people who share a characteristic protected by the equalities legislation and those who do not share it, or if there is information that could be collected during the assessment process which would enable NICE to take account of equalities issues when developing guidance.

Do you consider the technology 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 the technology 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)