NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Dabigatran etexilate for the treatment and secondary prevention of deep vein thrombosis and/or pulmonary embolism

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of dabigatran etexilate within its licensed indication for the treatment and secondary prevention of deep vein thrombosis and/or pulmonary embolism.

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 2 in 1000 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 (started as soon as possible) and a vitamin K antagonist (started within 24 hours). Treatment with low molecular weight heparin or fondaparinux should continue for at least 5 days or until an international normalised ratio of greater than or equal to 2 is reached, and treatment with a vitamin K antagonist should continue for 3 months or beyond depending on the person's risk of recurrent venous thromboembolism event and 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 Appraisals 261 and 287 recommend rivaroxaban as an option for treatment and prevention of deep vein thrombosis and pulmonary embolism, respectively.

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 two clinical trials of adults with acute symptomatic venous thromboembolism in comparison with warfarin. Dabigatran etexilate has 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 and has also been compared with warfarin in a clinical trial of adults who had a pulmonary embolism 3-12 months prior to trial entry and required secondary prevention of venous thromboembolism.

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 deep vein thrombosis and/or pulmonary embolism
Comparators	• Initial treatment with a low molecular weight heparin or fondaparinux and continued vitamin K antagonist • rivaroxaban For people with cancer • low molecular weight heparin • 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, heart failure and chronic thromboembolic pulmonary hypertension. • adverse effects of treatment (particularly bleeding, including intracranial and gastrointestinal 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	If evidence allows, subgroups will be considered by type of venous thromboembolism (pulmonary embolism or deep vein thrombosis). The analysis should consider both those who require a limited period of anticoagulation (3–6 months) and those who require long-term anticoagulation (usually lifelong). 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 of deep vein thrombosis and prevention of recurrent deep vein thrombosis and pulmonary embolism. Review proposal date May 2015. Technology Appraisal No 287, June 2013. Rivaroxaban for treating pulmonary embolism and preventing recurrent venous thromboembolic events. Review proposal 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: Quality Standard No 3, VTE prevention quality standard, June 2010. Quality Standard No 29, Quality standard for diagnosis and management of venous thromboembolic diseases, March 2013.