THERAPEUTIC AND ECONOMIC VALUE OF DABIGATRAN VERSUS WARFARIN
IN THE TREATMENT OF PATIENTS WITH ATRIAL FIBRILLATION

Background
Atrial fibrillation (AF) is associated with a risk of blood clot formation inside the heart and consequent tissue damage due to lack of oxygen (such as a stroke). Preventing the formation of cardiogenic blood clots (embolisms) with anticoagulant therapy (medication to prevent blood clotting) or by other means is the most important treatment with regard to the prognosis of patients with AF.

Warfarin has long been the most common anticoagulant medication and is still recommended in national treatment guidelines. In 2011, the marketing authorisation for dabigatran was extended to cover anticoagulation (prevention of blood clotting) in patients with AF who are at increased risk of stroke and whose AF is non-valvular, i.e. not related to the heart valves. The estimated number of AF patients in Finland is 50,000 to 100,000. A pilot assessment by the Finnish Medicines Agency (Fimea) has evaluated the therapeutic and economic value of dabigatran versus warfarin in anticoagulant therapy in patients with AF.

What are the practical differences between dabigatran and warfarin therapy?
There are significant differences in the practical aspects of dabigatran and warfarin therapies. The dosage of warfarin is individual and based on laboratory tests (INR readings). In dabigatran therapy, the dose is fixed and the same kind of laboratory follow-up is not required. When patients use dabigatran instead of warfarin, the healthcare and other resources for such follow-ups can be mobilised for other uses. One restriction of dabigatran therapy is that its effect cannot be reversed with an antidote, for instance when the patient experiences serious bleeding or needs surgery. The effect of warfarin, on the other hand, can be reversed if required.

What are the potential health benefits of dabigatran versus warfarin?
Evidence on the effects of dabigatran in the treatment of AF is mostly based on one study lasting an average of 2 years. Dabigatran at the higher dose (150 mg twice daily) was more effective in preventing strokes and systemic blood clots (11 cases in dabigatran therapy per 1,000 patient years compared with 17 in warfarin therapy). Dabigatran was also more effective than warfarin in reducing cardiovascular mortality. However, these differences were not observed with the lower dose of dabigatran (110 mg twice daily).

What are the potential health risks of dabigatran versus warfarin?
There were fewer cases of serious bleeding with the lower dose of dabigatran than with warfarin (29 cases in dabigatran therapy per 1,000 patient years compared with 36 in warfarin therapy). This difference was not observed with the higher dose of dabigatran. Serious gastrointestinal bleeding occurred more frequently with the higher dose of dabigatran than with warfarin (15 cases in dabigatran therapy per 1,000 patient years compared with 10 in warfarin therapy). However, this difference was not observed with the lower dose of dabigatran.
The rates of intracranial bleeding (bleeding inside the skull) were lower with both doses of dabigatran than with warfarin (3 such events per 1,000 patient years with the higher dose of dabigatran and 2 with the lower dose compared with 7 in warfarin therapy). On the other hand, myocardial infarctions may occur more often with both doses of dabigatran than with warfarin (8 such events in dabigatran therapy per 1,000 patient years, irrespective of whether the higher or lower dose was used, compared with 6 in warfarin therapy).

Dabigatran therapy was associated with more stomach complaints (dyspepsia) than warfarin. Such complaints occurred in 6% of patients on warfarin therapy and in 11–12% of patients receiving dabigatran. Patients using dabigatran stopped using the agent more frequently than those on warfarin. The reasons for stopping the medication varied.

**What are the situations in which dabigatran may have health benefits compared to warfarin?**

Dabigatran therapy is likely to have therapeutic benefits compared to warfarin when warfarin therapy is poorly controlled. If warfarin therapy is well controlled, the benefits of dabigatran therapy are likely to be less.

**Is dabigatran therapy cost-effective compared to warfarin?**

Dabigatran therapy involves considerably higher costs than warfarin. Dabigatran therapy is more likely to be cost-effective when warfarin therapy is poorly controlled. If warfarin therapy is well controlled, the benefits of dabigatran are low in relation to the higher costs.

**More research evidence and user experiences are required**

Research on the use of dabigatran in AF is still scarce and studies have been of limited duration. Patients and doctors also have relatively little experience of using dabigatran. The assessment of the therapeutic and economic value of dabigatran is therefore subject to limitations.

**Patient summary background**

This patient summary is based on an assessment by the Finnish Medicines Agency (Fimea) of the therapeutic and economic value of medicines. During the assessment, Fimea addresses the available clinical and health economics evidence. Healthcare professionals and those needing more detailed information on the matter are encouraged to read the full assessment report (The therapeutic and economic value of dabigatran compared with warfarin as anticoagulation in the prevention of stroke and systemic embolism in patients with atrial fibrillation.pdf, in Finnish).

**Disclaimer**

Assessments of the therapeutic and economic value of medicines are summaries of the health and economic effects of pharmacotherapy, compiled by experts. They do not replace a doctor’s or other healthcare professional’s own assessment and treatment decisions regarding the best possible treatment of an individual patient.

**What is Fimea?**

The Finnish Medicines Agency (Fimea) produces and compiles assessments on the therapeutic and economic value of medicines and coordinates the related collaboration. In Finland, medicines must have a marketing authorisation granted by Fimea or the European Commission. To obtain a marketing authorisation, the efficacy, safety and adequate quality of the medicine must have been demonstrated. Demonstration of the therapeutic and economic value of a medicine is not a prerequisite for a marketing authorisation. Evidence on the effectiveness and therapeutic and economic value of a medicine is used to support decision-making concerning the use of medicines.