

NICE TA 249: Atrial fibrillation - Dabigatran Etxilate

1	<p>Name of Commissioning Team</p> <p>Long Term Conditions Commissioning Team</p>
2	<p>Summary of NICE TA 249: Atrial fibrillation - Dabigatran Etxilate</p> <p>Dabigatran etexilate is recommended as an anticoagulant option for the prevention of stroke and systemic embolism within its licensed indication, that is, in people with nonvalvular atrial fibrillation with one or more of the following risk factors:</p> <ul style="list-style-type: none"> • previous stroke, transient ischaemic attack or systemic embolism • left ventricular ejection fraction below 40% • symptomatic heart failure of New York Heart Association (NYHA) class 2 or above • age 75 years or older • age 65 years or older with one of the following: diabetes mellitus, coronary artery disease or hypertension <p>It is <u>not</u> recommended for those with valvular AF.</p> <p>Dose depends on age.</p> <ul style="list-style-type: none"> • For those aged 80 or over a dose of 110mg twice daily should be used. • For those under 80 a dose of 150mg twice daily should be used. • For those aged 75-80, it is at the clinician's discretion as to whether 110 or 150mg dosing should be used. <p>The scale of any additional costs will depend on the degree to which GPs consider dabigatran to be clinically appropriate for a patient on an individual risk assessment, taking account of the risks and benefits outlined above.</p> <p>The introduction of this drug should be monitored carefully in view of the limited long term (ie >2 years) safety data available.</p> <p><i>Note: This service notification should be read in conjunction with the service notification for TA 256 & TA 275 which deals with the same cohort of patients.</i></p>
3	<p>Number of people in Northern Ireland expected to take up service/therapy (new cases per year)</p> <p>There were 27,213 adults with atrial fibrillation on GP practice registers in 2011/12. Over 90% (about 24,491) of these are estimated to have non valvular atrial fibrillation. The number of people on atrial fibrillation GP registers increases by c. 1000 patients per year.</p>

	<p>There were 538 prescriptions dispensed for dabigatran costing £46,749 between April 2011 to March 2012.</p>
<p>4</p>	<p>Outcomes</p> <p>Dabigatran is suitable for prescribing in primary care as an anticoagulant option for non valvular atrial fibrillation. NICE recommends that the ‘decision about whether to start treatment with dabigatran should be made after an informed discussion between the clinician and the person about the risks and benefits of dabigatran compared with warfarin. For people who are taking warfarin, the potential risks and benefits of switching to dabigatran should be considered in light of their level of international normalised ratio (INR) control’. In some patients, it is difficult to maintain an INR within the therapeutic range.</p> <p>NICE concluded that evidence for stratifying by INR control was insufficient to exclude the minority of people with very good control from the recommendation of dabigatran as a potential treatment option, and that therefore, their recommendation should apply to the whole population who meet the indications for treatment.</p> <p>NICE noted that both doses of dabigatran were associated with statistically significant reductions in the incidence of life-threatening bleeds compared with warfarin, particularly the risk of haemorrhagic stroke and intracranial haemorrhage. However, NICE also concluded that treatment with dabigatran resulted in more gastrointestinal bleeding than warfarin, which may be the result of a local effect of the orally administered drug on the gastrointestinal mucosa.</p> <p>Dabigatran 150 mg twice daily was associated with a statistically significantly lower incidence of stroke or systemic embolism, ischaemic stroke and vascular mortality compared with warfarin, but there were no statistically significant differences between dabigatran 110 mg twice daily and warfarin. The Committee concluded that dabigatran 150 mg twice daily was more clinically effective than warfarin in reducing the risk of stroke or systemic embolism, ischaemic stroke and vascular mortality and that this represented an important development for people with atrial fibrillation. It also concluded that the lower 110 mg dabigatran twice-daily dose had shown non-inferiority to warfarin.</p> <p>However</p> <ul style="list-style-type: none"> • No long-term (>2 years) safety data is currently available for dabigatran • It is a potent anticoagulant, thus it should be used with caution in patients at higher risk of bleeding, particularly very elderly or frail patients in whom bleeding complications may be serious • There is no specific antidote to dabigatran (unlike warfarin). • Bleeds associated with dabigatran are treated with human prothrombin complex. Platelet transfusions can also be used; the platelet stock in NI is small. • 1 death has been reported in N.Ireland to date.

	Overall, people with good INR control with warfarin, may not gain additional clinical benefit by taking dabigatran.																				
4.1	Additional life expectancy gain / progress improvement See section 4. It is an oral therapy which unlike warfarin does not require frequent drug monitoring or dose titration.																				
4.2	Reduction in morbidity In comparison to warfarin, 91 patients need to be treated to prevent 1 additional stroke or pulmonary embolism.																				
4.3	<p>Cost per patient per annum</p> <table border="1"> <thead> <tr> <th>Drug</th> <th>Dose</th> <th>Cost per month</th> <th>Annual cost</th> <th>Additional costs</th> </tr> </thead> <tbody> <tr> <td>Dabigatran</td> <td>150mg b.d</td> <td>£66.00</td> <td>£801.80</td> <td>Renal function as per MHRA guidance</td> </tr> <tr> <td>Warfarin</td> <td>As per INR</td> <td>£0.93-1.98</td> <td>£23.76</td> <td>Drug monitoring costs - >£2.03M/annum in primary care</td> </tr> <tr> <td>Aspirin</td> <td>75-300mg</td> <td>£0.83</td> <td>£9.96</td> <td></td> </tr> </tbody> </table> <p>Renal function as per MHRA guidance:</p> <ol style="list-style-type: none"> 1. Renal function should be assessed in all patients prior to initiating Pradaxa therapy 2. Pradaxa is contraindicated in patients with severe renal impairment 3. While on treatment renal function should be assessed in clinical situations where a decline in renal function is suspected 4. In elderly patients (>75years) or in patients with renal impairment the renal function should be assessed at least once a year. <p>Using the maximum additional cost of dabigatran compared to warfarin of £768/year/patient and 100% of patients selecting dabigatran, the maximum potential additional costs = £18.8m. The estimated costs are lower because a minority of patients are expected to actually be treated with this drug. See 4.6 for further details on estimated costs</p>	Drug	Dose	Cost per month	Annual cost	Additional costs	Dabigatran	150mg b.d	£66.00	£801.80	Renal function as per MHRA guidance	Warfarin	As per INR	£0.93-1.98	£23.76	Drug monitoring costs - >£2.03M/annum in primary care	Aspirin	75-300mg	£0.83	£9.96	
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4.4	In year cost per patient per annum £801.80/patient/year for dabigatran; £23.76/yr for warfarin; additional cost = £768/year/pt; in-year costs depends on the number of patients prescribed dabigatran rather than warfarin																				

4.5	<p>Cost savings and how these will be secured</p> <p>Dabigatran is £768/patient/year more costly than warfarin. The additional costs would be borne by the primary care prescribing budget.</p> <p>The anti-coagulation monitoring payments made to GP practices, and fixed costs associated with secondary care monitoring may reduce with time, but are likely to be modest as it is likely that the majority of patients (80%) will remain on warfarin; this will need to be kept under review.</p>
4.6	<p>Recurrent overall cost</p> <p>See section 4.5 for details.</p> <p>There is a maximum annual cost of £4.5m as per NICE costing template based upon 25% eligible patients choosing rivaroxaban. The net cost based upon the NICE costing template was £736K. These costs are based upon NICE estimates on unit costs.</p> <p>It should be noted that these net additional costs are dependent on the realisation of event reductions which may be affected by other parameters. The costing template does not take into account an increase in the size of the target population i.e. older people.</p> <p>The manufacturer has agreed that dabigatran will be available to the NHS with a patient access scheme in which a discount is applied to all invoices. The level of the discount is commercial in confidence. Trusts in Northern Ireland will be expected to avail of this scheme.</p>
4.7	<p>Cost per QALY</p> <p>£18,900 (<80 years of age)</p>
4.8	<p>Other treatments available for this condition</p> <p>Warfarin Newer agents on the horizon e.g, apixaban, edoxaban, betrixaban</p>
4.9	<p>Readiness to implement</p> <p>There will be a managed process to communicate the risks and benefits of Dabigatran to GPs and secondary care primarily, through:</p> <ul style="list-style-type: none"> ▪ PCP Clinical Leads ▪ Practice-level reports providing comparisons of prescribing rates with peers, and trends ▪ Medicines Management advisers routine visits to practices & encouraging practices to use the NICE TA audit where appropriate. <p>GP educational events</p>

	<p>Secondary care clinicians often initiate treatment and maintenance treatment is overseen by primary care, common protocols (including what how to manage associated bleeding) need to be developed between primary and secondary care at Trust level.</p>
5	<p>DHSSPS Legislative / Policy Caveats</p> <p>This advice does not override or replace the individual responsibility of health professionals to make appropriate decisions in the circumstances of their individual patients, in consultation with the patient and/or guardian or carer. This would, for example, include situations where individual patients have other conditions or complications that need to be taken into account in determining whether the NICE guidance is fully appropriate in their case.</p>
6	<p>What will the Commissioning Team do to secure funding for the implementation of this TA including any proposals for disinvestment</p> <p>Any cost pressure will appear in the primary care prescribing budget. The potential savings to Trusts should be calculated pro rata according to the degree of use of dabigatran and offset against other Trust cost pressures.</p>
7	<p>Commissioning arrangements</p> <p>As outlined in this statement.</p>
8	<p>Monitoring arrangements</p> <p>The prescribing trends for this budget will be monitored closely by:</p> <ul style="list-style-type: none"> ▪ Practices and GPs in the prescribing scheme ▪ ICP and LCG Leads ▪ Medicines Management advisers ▪ The Medicines Management Commissioning team.