

Issue 1 Failure to address the population problem of poor uptake of anti-coagulation amongst high risk patients

Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)
<p>The guideline needs to take greater account of the current major community health problem of inadequate management of AF.</p> <p>There has been poor implementation of the NICE 2006 AF guideline on anti-coagulation.</p> <p>This is illustrated by work carried out interrogating GP databases using the GRASP-AF tool. Uploaded information is available from some 868 practices totalling a population of over 6 million patients, some 108,000 with AF. Amongst high risk patients (CHADS > 1), 45.8% were not receiving an oral anti-coagulant. A contra-indication to anti-coagulation was recorded in only 35.5% of this untreated group.</p> <p>Barriers to warfarin appear to include the accessibility of frail and elderly patients to anti-coagulant monitoring, the ability of some patients to cope with variable warfarin dosing and the attitudes of both medical staff and patients to warfarin.</p> <p>Dabigatran presents a very real opportunity to overcome at least some of these barriers.</p>	<p>Consideration needs to be given to alternative comparators to warfarin.</p> <p>Amongst patients who for a wide variety of reasons cannot take warfarin, a more appropriate comparator would be aspirin. There should therefore be a reappraisal of the cost efficacy of dabigatran therapy in comparison with aspirin for patients amongst whom warfarin therapy is inapplicable. This could be achieved by combining the results of the RELY and BAFTA studies.</p>	<p>We do not think that this amendment can be fitted into the current model.</p> <p>An alternative illustration is provided. This was prepared for the West Yorkshire Cardiovascular Network by York Health Economics Consortium.</p> <p>This analysis was based on combining results from RELY and BAFTA and hence was based on a number of assumptions. It was limited to patients over the age of 75.</p> <p>The base case incremental cost per QALY was £4820 for dabigatran 150mg and £10,050 for dabigatran 110mg, both in comparison with aspirin.</p> <p>In population terms, extrapolating from the GRASP data, there are over 250,000 patients nationally with AF and known risk factors at high risk of stroke who are currently not treated with an oral anti-coagulant. If these patients were treated with any anti-coagulant, it would offer the potential to reduce stroke rates in the UK by some 4800 strokes each year. Dabigatran and the other new anti-coagulants offer the possibility for a major new initiative in stroke prevention in providing therapy for patients who currently cannot access warfarin services.</p>

Issue 2 Additional consideration of the benefits of dabigatran in relation to time in therapeutic range on warfarin

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<p>The current ACD does not adequately explore the importance of time in therapeutic range. This issue is of such magnitude that it is likely to dwarf other issues, such as the cost of anti-coagulation monitoring with warfarin, which have been highlighted.</p> <p>The current ACD also fails to consider to what extent the population in RELY is comparable with the UK population in quality of anti-coagulant control. Amongst countries which contributed patients to the RELY study, the UK was fifth best for quality of anti-coagulant control. The mean TTR for UK centres was 72% compared with a median of 65% for the study as a whole.</p>	<p>We would recommend that the model is rerun, based on the quartiles of time in therapeutic range with warfarin in the RELY study, presented by Wallentin et al.</p> <p>More information is required on the distribution of time in therapeutic range amongst UK patients. We believe that some information may be available from the manufacturers of anti-coagulant management guidance software which would help inform the significance of this proposal in terms of the number of patients eligible for warfarin therapy based on poor time in therapeutic range.</p>	<p>The York Health Economics Consortium model carried out for the West Yorkshire Cardiac and Stroke Network gave the following results.</p> <p>Cost per QALY for dabigatran compared with warfarin</p> <table data-bbox="1503 667 2047 933"> <thead> <tr> <th></th> <th>150mg</th> <th>110mg</th> </tr> </thead> <tbody> <tr> <td>Base case</td> <td>£12640</td> <td>£31315</td> </tr> <tr> <td>TTR < 56.9</td> <td>£2800</td> <td>£8720</td> </tr> <tr> <td>TTR 56.9-65.4</td> <td>£5165</td> <td>£19450</td> </tr> <tr> <td>TTR 65.4-72.4</td> <td>£29354</td> <td>£18990</td> </tr> <tr> <td>TTR > 72.4</td> <td colspan="2">Warfarin more cost effective.</td> </tr> </tbody> </table> <p>It seems probable therefore that considering different TTR ranges will have a very major effect on the conclusions of the ACD as to cost efficacy in different patient groups and we would encourage the appraisal to pursue this issue further.</p>		150mg	110mg	Base case	£12640	£31315	TTR < 56.9	£2800	£8720	TTR 56.9-65.4	£5165	£19450	TTR 65.4-72.4	£29354	£18990	TTR > 72.4	Warfarin more cost effective.	
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Issue 3 Insufficient attention to disadvantaged patient groups

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<p>Many patients cannot take warfarin for reasons other than simple bleeding risk. This can be for a variety of reasons including, poor mobility and frailty limiting access to anti-coagulant monitoring services and impaired mental capacity causing difficulties in variable drug dosing.</p> <p>It is unethical to deny these patients a potentially highly cost effective treatment</p>	<p>As already discussed, aspirin may be a more appropriate comparator for some of these patient groups.</p> <p>Alternatively, the model should consider that it is unlikely that there is a single, unique cost of anti-coagulant control with warfarin. For example, the costs are likely to be substantially higher in a patient who requires domiciliary visits for blood sampling or who requires direct supervision of variable warfarin dosing.</p> <p>The model therefore needs to be amended to ensure that the full costs of anti-coagulant control in disadvantaged groups are considered.</p>	<p>The results are likely to reduce the incremental cost of dabigatran in comparison with warfarin amongst disadvantaged patients</p>

(please cut and paste further tables as necessary)