

Response by Atrial Fibrillation Association to NICE Appraisal for
Dabigatran etexilate
for the prevention of stroke and systemic embolism in Atrial Fibrillation

AFA is mindful that budgetary pressures within the NHS are ever-present and inevitable, and as a result, cost effectiveness has to be a reasonable expectation before new therapies can be recommended. However when comparing treatments it is important not to just consider cost but also effectiveness and this should take into account the wide gap between clinical trial data and real clinical practice. While this difference has been recognised for some time it is probably best summarised but the QIPP, Right Care programme, 'Commissioning for Value':

'value must also be measured by outputs, not inputs. Hence it is patient health results that matter,'

The AFA has amassed and documented the experiences of a vast number of patients and health care workers that have been shared with us. These accounts are a true representation of the "health results" of patients suffering from AF in the UK today. In light of this amassed patient feedback and respected published data we have formulated the following summary of point on behalf of patients suffering from AF:

- 1) AF is the greatest risk factor for stroke and results in more severe strokes**
- 2) Patients with AF are not prescribed appropriate stroke prevention in the vast majority of cases**
- 3) The main reasons for this are patient and physician resistance to using warfarin.**
- 4) For those patients on warfarin large numbers of patients are difficult to control and spend >60% outside the target therapeutic range – rendering warfarin of no benefit.**
- 5) The NHS should use warfarin as the first choice therapy but must accept that many will have expensive strokes if an alternative is not available for those patients unable to maintain INR**
- 6) The committee does not have representation from all relevant professionals**

We present arguments for these points in more detail as follows.

1) AF is the greatest risk factor for stroke

Atrial Fibrillation is known to be responsible for 45% of all embolic strokes, resulting in more than 12,500 strokes per year in England and Wales. AF strokes are usually more severe and cause more death and disability. The medical cost of a stroke in first year is £9,500 - £14,000 per stroke. Embolic strokes are likely to be represented at the high end of this range.

Hospital stay costs following a stroke are £103 million and post-discharge care, £45 million. These costs do not include continuing costs after first year, nor do they include costs associated with long term disability or the human cost, which is incalculable. The well-documented and persistent failure of warfarin adequately to reduce stroke risk results in thousands of preventable ischemic strokes attributable to AF. The AFA suggests that these preventable strokes should be factored into the QAL.

2) Patients are not prescribed appropriate stroke prevention

In clinical trials warfarin has been associated with a stroke risk reduction in AF patients of 50%-70%. However, this potential is not being realised in routine clinical practice, leaving thousands at risk of preventable strokes. Warfarin is under-prescribed for many reasons including the complexity of dosing and patient management as well as fear of the associated bleeding risks. Consequently, almost half the AF patients for whom warfarin is indicated are not on warfarin and remain at extremely high risk of severe, debilitating and expensive strokes.

3) The main reason for lack of stroke prevention is patient and physician resistance to using warfarin

Management of warfarin is complex and time-consuming for primary care physicians who currently gain equal financial reward for prescribing aspirin to tackle stroke prevention in AF patients. There is therefore great incentive against prescribing warfarin. It is also recognised that those at greatest risk, the elderly, are less likely to be given warfarin because of perceived fear of complications. However although the ERG had been tasked to consider QAL for AF patients 75+, there are large numbers of younger patients who according to NICE guidance should also be prescribed anticoagulants including 'those with a history of stroke and those aged 65 years or over with one of the following: diabetes, coronary artery disease, or hypertension.' The AFA has collected survey evidence from this age. Of those still in employment, 54% reported that warfarin had a very high impact on their job and employment. This will be increasingly relevant as the age of the population and retirement ages increase.

4) For those patients on warfarin large numbers of patients are difficult to control and spend >60% outside the target therapeutic range – rendering warfarin of no benefit.

As few as 18% of AF patients are adequately treated to prevent stroke. Estimates vary but only 60-70% of AF patients are thought to be diagnosed in the UK. Of those, 97% are considered at moderate or high risk, and hence in need of anticoagulation therapy according to the most recent international expert consensus guidelines. Of patients indicated, NICE's own review of the literature in 2006 concluded that only 54% actually receive warfarin. Published evidence on the amount of time patients spend in therapeutic range indicate that of warfarinised AF patients, only 56% are within range at any one time.

As simple combination of these numbers suggests that at any one time, warfarin is effectively and safely reducing stroke risk in only 18-21% of AF patients.

5) The NHS should use warfarin as the first choice therapy but must accept that many will have expensive strokes if an alternative is not available

AFA strongly believes that comparison of dabigatran with well-controlled warfarin is ignoring the cost of stroke those patients in whom warfarin is ineffective or impossible to use. A fair comparison is therefore to aspirin or to nothing. Therefore denial of a new, safe and more effective treatment for these AF patients is not based on a fair appraisal. We would propose that dabigatran should be recommended for the following patients if they are at moderate or high risk of stroke according to the CHADS₂VASc₂ system:

- a) those in whom warfarin is poorly controlled (<70% time in therapeutic range) or in whom complications result from poor control (bleed/TIA/stroke)
- b) those for whom warfarin INR monitoring will limit their opportunity to access work, maintain employment and access promotion

7) The committee does not have representation from all relevant professionals

The oral anti-coagulants are largely prescribed by and managed by primary care physicians, however in reviewing dabigatran, this group of physicians was not represented. Neither were commissioners who, without guidance issued by NICE, will face considerable pressure. The AFA calls upon the committee to include representation from Primary Care and Commissioners.

Conclusions:

AFA does not believe that the current recommendations are sound or that they represent as a suitable basis for guidance to the NHS. An NHS priority is to reduce the number of strokes. The current recommendations act against this priority, despite trial evidence (RE-LY) and expert witness statements, given before and at the appraisal meeting. AFA believes that this will result in:

- Continued rise in the event of strokes due to AF
- Conflicts between patients and clinicians
- No local guidelines, leading to inequality of services and care and cost inefficiencies
- Promotion of unwarranted inequalities in stroke risk reduction

AFA calls upon the Committee to issue guidance on dabigatran with consideration to the points AFA has highlighted in its response to the appraisal consultation document.