Response by Atrial Fibrillation Association to NICE Appraisal for Rivaroxaban 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 to not only consider cost but also effectiveness. These considerations 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 by 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,'

1. AF is the single most powerful risk factor for stroke, increasing an individual's risk of stroke by nearly 500%.[1] Consequently, antithrombotic therapy should be considered routine in most people with atrial fibrillation.

2. Strokes as a result of AF are considerably more severe than non-AF strokes. AF-related strokes result in greater disability, social dependency and death;[2,3] they are more expensive[4] and they are more likely to recur in the absence of effective treatment.

3. Current guidelines recommend that 97% of AF patients should be prescribed an oral anticoagulant (OAC) to ensure adequate reduction of stroke risk.[5] Yet, data from the National Institute of Health and Clinical Excellence (NICE) indicates that only 54% of AF patients in need of OAC treatment are receiving treatment.[6] Even accounting for those unsuitable for OAC therapy, this represents vast under-utilisation of life-saving anticoagulation treatment.

NICE comments that more than 166,000 known AF patients should be on OAC but are not.[7] Given that AF is directly responsible for 12,500 stokes in the UK each year,[8] a clear opportunity to save thousands from death and disability is being missed by a significant margin.

4. For the last 50 years, a group of drugs called the vitamin K antagonists (VKAs) have been the mainstay of OAC treatment. Of these drugs only one, warfarin, is used routinely in clinical practice. Multiple clinical trials have shown that well-controlled, dose-adjusted warfarin is a safe and effective therapy, having been shown to reduce the risk of stroke in AF patients by up to 68%.[9,10,11] However, warfarin has a narrow therapeutic range and it interacts with many common foods and medicines. Consequently, warfarin requires close monitoring and frequent dose adjustments to ensure that patients receive a dose that consistently maintains a reduced risk of stroke without increasing the risk of bleeding.

   "*You have to visit the hospital very regularly, sometimes every week or every fortnight if the drug does retain the normal therapeutic level, but more often than not, it fluctuates*." **Evelyn, 89**

5. Despite the wealth of clinical trial evidence, warfarin is only prescribed for 54% of those in need of it[12] and, among those on warfarin, only 56% are found to be within therapeutic range.[13] As a result, a significant majority of AF patients, in need of OAC, remain at high risk of stroke.

   "I worry if I have a glass of wine on a Sunday with my daughter, or if I eat green vegetables. I love sprouts but they have been such a problem." **Alice, 59**

The challenge is to effectively reduce the risk of stroke in key groups of patients with AF:

i) Those among the 45% not receiving the OAC therapy that they need;[14]

ii) Those among the 44% not currently within the therapeutic range of warfarin;[15] and

iii) Those unable to tolerate warfarin therapy.

In light of this, AFA does not believe that the current recommendations are sound or that they represent 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 (ROCKET-AF) 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 NICE committee to issue guidance on rivaroxaban with consideration to the considerable challenges of current therapy options, and mindful of the vulnerable AF patient groups at high risk of stroke. These patients could be summarised as those with a CHADS2Vasc score of 1 or more and poorly controlled on warfarin (<60% of time in therapeutic range) or allergic/intolerant of warfarin. These might include both true allergies and side effects or:

- Individuals with multiple risk factors and, hence, on polypharmacy causing considerable issues to successful and safe management of warfarin therapy
- Those intolerant of warfarin
- Individuals who are unable to manage multiple doses who also require regular review and likely changes to their doage
- Those living within care settings where drug management relies upon non-medical staff reluctant to support management of difficult medication which can be potentially life threatening
- Those who are liable to dose error due to mental health issues

- Those who are needle phobic
- Those with limited ability to attend monitoring appointments such as the immobile, those in care homes and those living in rural areas
- The most vulnerable patients such as the elderly, who are often at greater risk both of stroke and by multiple risk factors, polypharmacy, dementia, non-adherence to therapy and by inconsistencies in approaches to anticoagulation management throughout the health service.
- Those who struggle and are simply unable to manage warfarin successfully due to work and lifestyle issues

The importance of these lifestyle changes was recently endorsed in a statement from the British Medical Association,

> *"...It is all well and good to say that everyone with atrial fibrillation should be on warfarin, but the reality is that patients do not always want it ... Warfarin is not always right for patients – warfarin can be very dangerous for patients, and we have to make the right choice for the patient***."** **BMA 2011**[16]

In conclusion,

Little can be done to prevent Atrial Fibrillation or to reduce personal risk of stroke due to AF. Therefore managing this risk is paramount.

Aspirin in high risk AF patients is inadequate.

Warfarin is currently the only option, and this is neither successful nor suitable for all those at risk, an alternative is desperately needed.

We would also suggest that it is likely that dabigatran will be approved in some form for prevention of stroke in AF. Competition is important to the NHS to drive down prices and therefore having competitive OAC approved by NICE is going to improve value for the NHS.

AFA asks the Committee to act to protect these vulnerable patient groups and issue guidance for Rivaroxaban in the prevention of stroke and systemic embolism in Atrial Fibrillation.

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