Response from the British Association of Stroke Physicians to the NICE Appraisal Consultation Document for the Single technology appraisal: Rivaroxaban for the prevention of stroke and systemic embolism in people with atrial fibrillation

1. ITT vs. safety-on-treatment (see paragraph 4.3)

   We agree that for a non-inferiority study, the most conservative analyses are the 'per protocol' or the 'safety-on-treatment' patients (the former the most conservative), in order to test that the OR/HR/RR =1. However, the most conservative analysis for the superiority analysis is the intention to treat population. As the superiority estimates are used to populate the model, it would seem more reasonable to use the ITT population (as one would do for any other drug), rather than safety-on-treatment to make estimates about the efficacy in a population.

2. Underuse of effective anticoagulation

   Not all those with high risk of stroke and AF are treated with warfarin, to a large degree because of patient or doctor concerns. The proportion of these patients who would take rivaroxiban instead is not made explicit. The likely preference of warfarin refusers for the convenience of rivaroxaban could be made explicit in sensitivity analyses. It is in these patients that the real advantage of a drug that needs no monitoring might be seen (though they are unlikely to have taken part in ROCKET-AF).

3. Weighting of bleeds

   A major clinical concern to stroke physicians is the risk of ICH with treatment. There is a very small difference in these proportions between rivaroxaban and warfarin. However, stroke physicians will know of the different average severities of ICH and ischaemic strokes, though the weighting applied to ICH in the models is redacted.

4. Paragraph 3.7

   The last sentence draws inappropriate attention to a difference in the p value of 2 post-hoc subgroup analyses; it seems unlikely that there is an interaction in treatment effect by prior use of vitamin K antagonists.

5. Age as a risk factor for all adverse outcomes

   Age is a plausible risk factor for all the adverse outcomes mentioned in paragraph 3.13.

6. Paragraph 3.18

We agree that the health care costs of TIA should enter model, though we think that the health weighting of these events is very small (and are not convinced this has been reliably estimated).

7. Paragraph 4.5

   Anticoagulants don’t control AF, but rather mitigate its thrombolembolic complications.