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## **Consultee comment on appraisal consultation document**

### **Ticagrelor for the treatment of acute coronary syndromes**

Dear Professor Longson,

I am responding on behalf of NHS Oxfordshire to your letter inviting comments on the ACD for ticagrelor in acute coronary syndromes (ACS) from the point of view of an NHS commissioning body. NHS Oxfordshire regrets that it was not invited to give a commissioning viewpoint at the appraisal meeting, although we do not doubt that NHS Bradford and Airedale was able to offer opinions which reflected the needs of the NHS.

As a commissioning organisation we are primarily interested in: how guidance will need to be implemented by our providers, including; the need for service changes and training, will the technology offer the anticipated benefits in the real world, are the full costs of treatment including those associated with adverse events captured in the cost-effectiveness analysis, is the wording of the guidance specific enough for us to reach agreement with our providers, are relevant stopping criteria included and can the implementation of the guidance be easily monitored and audited. The specific responses in this letter are based upon those requirements.

We are aware that the issues of affordability and opportunity costs which are of great importance to NHS commissioning bodies are specifically outside the remit of NICE, as stated in paragraph 4.12 of the Appraisal Committee's deliberations, but would like to take this opportunity to state that we wish it were otherwise.

#### **Evidence of clinical and cost-effectiveness**

NICE asks if all the relevant evidence has been taken into account. We are content that the PLATO study with its attendant sub assessments is the relevant trial and that no other evidence has been missed. We have also looked at the quoted costs for treatment which are put forward within the manufacturer's submission and they appear to be an accurate reflection of NHS costs which accrue in ACS.

We paid particular attention to the comparison of costs between clopidogrel and ticagrelor because of the considerable variation in the 12 month costs of the drugs (quoted as £42.16 and £713.70 respectively). The cost-effectiveness argument therefore relies upon the anticipated reduction in vascular events seen in the PLATO trial and, as far as we could tell this was accurate.

We have concerns regarding the adverse event profile and its incorporation into the costs (page 14 of 292 in the manufacturer's submission dated 12<sup>th</sup> November 2010) taken from the trial. If the incidences of bleeding and dyspnoea in general use result in more referrals (as they could

since trial patients will be more intensively monitored than in general practice) then the costs will be higher than in the trial. This would impact adversely upon the cost-effectiveness. However, we are unable to make an estimate of increased costs.

## **Are the provisional recommendations sound and a suitable basis for guidance in the NHS?**

Ticagrelor has a rapid onset of action and equally rapid reversibility. Whilst this can be an advantage for patients before surgery, it does mean that for the patient to achieve benefit they must comply with treatment. We understand that patients were admitted to the trial only if they were likely to be able to comply, and that the trial (Section B1, page 2 of 31 in the manufacturer's clarification letter to NICE dated 17<sup>th</sup> December 2011), employed methods estimating compliance. Consequently we disagree somewhat with the Appraisal Committee's conclusion in paragraph 4.6 that "decreased compliance would be unlikely to significantly reduce the effectiveness of ticagrelor plus aspirin relative to clopidogrel plus aspirin in the real world setting". It is because ticagrelor has a more rapid reversibility that compliance with ticagrelor compared with clopidogrel is of greater significance.

In the 'real world' compliance with long term medications has generally been accepted as about 70% (there is a broad range). We would like to see an addition to criterion 1.1 stating that use should be limited to patients who have been counselled on the importance of compliance with the treatment regime.

We would also request that it is made explicit, within the criteria for recommendation for use within the NHS, that treatment should not be continued for more than 12 months in line with the PLATO study and the posology section of the Summary of Product Characteristics. We base this upon our local experience of the use of clopidogrel for the prevention of vascular events following ACS, when GPs found it difficult to know if they ought to stop therapy, without specific guidance to do so.

## **Discrimination and equality issues**

We have found no aspects relating to unlawful discrimination or equality related issues.

## **Additional Points**

It would be helpful if, when quoting risks and benefits, the commentary on the consideration of evidence would always make clear when a figure is that of the relative risk or the absolute risk. Paragraph 3.3 states "patients in the ticagrelor group were 16% less likely to experience a primary end point". This is a relative risk reduction – the same paragraph later is explicit when using absolute risk reduction.

Oxfordshire PCT has been grateful for this opportunity to participate in the NICE process for this technology.

Yours sincerely

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