NHS
Airedale, Bradford and Leeds

22nd Feb 2012

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Jeremy Powell
Project Lead
National Institute of Clinical Excellence
By email.

Dear Jeremy

RE: Abiraterone for castration-resistant metastatic prostate cancer previously treated with a docetaxel-containing regimen

On behalf of the Shadow Clinical Commissioning Groups in Bradford and Airedale, and NHS Bradford and Airedale I would wish to offer the following comments in support of the ACD on Abiraterone in the above indication.

1 Clinical effectiveness evidence

Evidence for clinical effectiveness is based on a single high-quality phase III RCT (COU-AA-301). The primary outcome of this study was overall survival, the committee concluded this trial provided evidence that abiraterone offers a survival advantage to patients, compared to placebo. However, it is a single trial. As has been seen in many other new medicines there seems to remain significant uncertainties about how the trial effectiveness plays out in real life.

a) We concur with the advice given to the committee by clinical specialists that participants in COU-AA-301 were likely to be healthier than those who would receive abiraterone in the UK clinical practice, therefore would raise questions about the generalisability of the study to the UK. The manufacturer carried out a sub-group analysis on patients who had received only one prior chemotherapy regimen; the committee deemed this inappropriate as there was no evidence suggesting a difference in the clinical effectiveness of abiraterone in this subgroup.

b) We note the main finding of the net OS advantage (**compared to placebo** – hardly a high bar) of 4.6 months. However we note that the appraisal committee found no **robust evidence was available to compare the clinical effectiveness of abiraterone with its main clinical comparators or best supportive care. We concur that the main active comparator** mitoxantrone is rarely used in UK but that best supportive care is absolutely an appropriate comparator. This is of additional note when you consider that there is published research comparing active treatment and palliative care (lung cancer, NEJM 2010, reference available if required) highlighting that patients receiving early and high quality palliative care experienced less depression, improved quality of life and survived 2.7 months longer than standard care. Though obviously there are differences in biological mechanisms it clearly established that palliative care (which might conceivably be considered Best Supportive Care, and which funding may be reduced for should commissioners be required to fund this treatment) can and does have a clinically important impact. Therefore we believe it is an absolutely relevant comparator when considering the comparative clinical (and cost) effectiveness.

c) given the seeming issues re lack of external validity to the UK population and the lack of comparison to an active comparator, both noted above, this finding of Overall Survival advantage of 4.6 months does not seem particularly credible in the UK population.

2 Cost effectiveness

a) We concur with the Appraisal Committees view that the manufacturers estimation of £63,200 per QALY is likely to be an underestimate of the true value for money.- it would seem obvious that a manufacturer would populate a model with more optimistic assumptions. In addition, given the points raised in point 1c (above) it might be considered inappropriate to simply plug an OS advantage of 4.6 months into an economic model. This, in our view, further and significantly weakens the credibility of the manufacturers presentation of the ICER.

b) The ICER figure of £63,200 includes an agreed patient access scheme involving a single confidential discount to the list price of abiraterone. Whether the NHS commissioner (whom ultimately is financially responsible for the investment) actually realizes that discount in cash seems debatable, there are many examples of patient access schemes

that, whilst seeming like a good idea within the Department of Health, do not seem to actually work in practice. We can provide examples if the committee would wish.

c) In addition, commissioners and providers need to invest (sometimes substantially) in admin resources to make such schemes work – obviously this expenditure may have the net effect of cancelling out any savings that might be seen from the confidential reduction in list price (if indeed it is realized). We would expect that the requirement for additional expenditure on administration to make the PAS work would be reflected or at least taken into account in economic modeling.

3 End of life Criteria

a) We agree that this medicine is not licensed for a small population – estimates of ,690 in 2012 increasing to 4,214 in 2016 for the indication currently under consideration but the committee heard this may be an underestimate. **Thus it seems exceptionally hard to make a case that this indication would meet the end of life criterion.** Even if the EoL criterion did apply, the ICER would still likely be too high to qualify.

4 Potentially eligible population / impact on commissioners / opportunity cost

a) We would strongly encourage the Appraisal Committee to consider the population impact in epidemiological terms.

b) Particularly we would wish to draw attention to the impact on other patients affected by the opportunity cost of a requirement to fund this medicine were the Appraisal Committee to change their initial view

c) Manufacturer data (again we would view these to be optimistic under estimates) between six and seven (6.59) per 100,000 people are eligible for treatment with abiraterone annually for this indication at a cost of about £164,911. These figures include the drug cost of abiraterone at £2,930/month (list price) with treatment lasting an average of 8 months and a one off monitoring cost of £1,587.72 per patient. The annual cost per patient for the drug and monitoring is £25,028.

d) In 2013-16 the manufacturer predicts a small rise in the number of eligible patients to between 7 and 8 (7.32) per 100,000 people annually, giving a higher cost of

approximately £183,200 per 100,000. This would represent a budget impact of c£1m in Bradford and Airedale. We agree with the committee's conclusion that the appraisal should refer to people rather than men because people, who have proposed, started or completed male to female gender reassignment can develop prostate cancer. This is especially important to note as the cost per 100,000 figures above refer to people and not just men.

(We accept that these figures do not include the patient access scheme discount (redacted in the evaluation report) or the net budget impact of introducing abiraterone on existing treatments (estimated in the manufacturer's submission).

e) In epidemiological terms, taking into account response rates, OS advantage and those that do gain benefit AND those that don't, this investment would allow 17 men to have a chance of extending life by two to four months above current or no treatment respectively.

f) NHSBA currently (10/11 Programme Budget Data) spends £51m on cancer. Thus a spend of c£1m on medicine equates to almost 2% of the cancer budget spend on one medicine that effectively buys an upper estimate of four months additional survival in those 17 men.

g) This additional expenditure would come at a time when there is absolutely no growth in the NHS, and expectation a net effect (accounting for population growth and demographic change) of £50m being taken out of the baseline budget over the next few years.

h) For this level of expenditure, it seems reasonable to expect this medicine to have a significant effect on survival, life expectancy and possibly mortality rate for prostate cancer. Particularly given the inherent opportunity cost of other treatments forgone.

i) We understand and respect the fact that NICE is precluded form considering absolute affordability of its recommendations. However, NHS commissioners (and providers) MUST be mindful of this, indeed it is an absolute duty on PCTs who do not operate in a QALY based method of assessing value - the method is more one based on absolute cost and absolute value in a whole population. Thus opportunity cost is an all consuming factor.

j) The opportunity cost would fall on other, anonymous, patients if commissioners were required to make funding available to the relatively small no of patients who would get marginal benefit from this treatment.

h) Therefore, when deliberating this further. We would encourage the committee to be mindful of the services that would be reduced in order to make this treatment available. This would inevitably be in treatments that are more cost effective and highly valued by patients than this particular treatment. Inevitably it would seem that this would represent a net social loss of health, and we would encourage the committee to question whether this would be socially acceptable.

5 In summary

a) We would view this treatment to be of exceptionally High marginal cost for marginal clinical benefit for a tiny proportion of patients. With great opportunity cost, This seems exceptionally poor value to the taxpayer.

b) We note that this indication has recently been recommended by AWMSG and that the Welsh don't have the Cancer Drugs Fund as a let out valve for poor value medicines. Whilst we recognise that the CDF is top sliced from NHS Commissioners baseline budgets, those NHS Commissioners have little to no control over this. We would be of the view that this medicine ONLY has a place as a candidate (alongside many other medicines of poor cost effectiveness) for consideration within the CDF. However we would even question its place there. That would clearly be a decision beyond the remit of a NICE TA. **Certainly our view is that this medicine should have no place in being funded as part of NHS pathway that NHS commissioners have influence over**

c) Finally, we are aware of additional information that has been submitted by the manufacturer at a late stage. We have not seen this, and as such are blind to any implications in might have for the views we express here. We would hope to be able to review this additional information.

I would be more than happy to discuss this further with the committee if required.

Yours sincerely

[redacted]