ICR
The Institute
of Cancer Research

[redacted]

Jeremy Powell, Esq
Project Manager
The National Institute for Health and Clinical Evidence
MidCity Place
71 High Holborn
London
WC1V 6NA

24 February 2012

Dear Mr Powell

RE: Prostate cancer (metastatic, castration resistant) - abiraterone (following cytoxic therapy): appraisal consultation.

The Institute of Cancer Research (ICR) is grateful for the opportunity to comment on the Appraisal Consultation Document (ACD) for abiraterone in the treatment of metastatic, castration resistant prostate cancer, following cytoxic therapy. We are, of course, greatly disappointed by the draft recommendations contained in the ACD and hope that the Appraisal Committee will reconsider its position.

The ICR is one of the world's top four cancer research institutes, funded by a combination of public money and charitable contributions and we enjoy a very close association with the Royal Marsden NHS Foundation Trust.

Abiraterone was discovered by the ICR in its laboratories, in what is now the Cancer Research UK Cancer Therapeutics Unit, and ICR and the Royal Marsden carried out initial clinical development. Despite the Institute having licensed the drug, we did so under an arrangement that results in sales royalties being paid to us. These royalties go to fund future scientific research and drug discovery and development at ICR.

It is perhaps worth noting that people who have reached the advanced stage of prostate cancer, that is of concern to us in this case, would have few options open to them, beyond palliative care, if abiraterone were not to be made available. It appears to us that all parties have agreed that abiraterone is a highly effective and well tolerated therapy. Its launch was the culmination of many years of ground-breaking work by scientists and clinicians across the world. Abiraterone represents a major breakthrough in the treatment of advanced prostate cancer, with results of a major Phase III trial showing that patients given abiraterone lived on average 15.8 months compared to 11.2 months for men taking a placebo.

We believe therefore that it is crucial that some combination of the Department of Health, NICE and the manufacturer reach an accommodation acceptable to all parties to ensure that

this drug is made available and that patients can gain the unquestioned benefit of abiraterone.

The ICR is aware that NICE must take into account both the clinical and cost-effectiveness of a drug when conducting its appraisals. We do, however, have a number of concerns about certain aspects of the ACD and we deal with these in turn below.

First, in section 4.7 of the ACD, the Committee rejects the validity of the base-case population presented by the manufacturer. The Committee's view appears to have been based upon the lack of a statistically significant difference in overall survival between the subgroup presented by the manufacturer as its base-case (the 1 prior chemotherapy group) and the remaining patients in the trial (the more than 1 prior chemotherapy group). It is interesting to note, however, that the cost-effectiveness results for the subgroup and the overall patient population are markedly different (at least on the basis of the manufacturer's analysis and the Evidence Review Group report). It is therefore odd - and arguably irrational - for the Committee to state that it is 'unnecessary for the manufacturer to restrict the base-case population to this patient subgroup.'

Given the Committee's subsequent recommendations in the ACD against the use of abiraterone in the whole patient population, it would seem reasonable for it at least to re-examine fully the potential for abiraterone to be cost-effective in this subgroup of patients and we request that this work is undertaken prior to the issuing of a Final Appraisal Determination.

Second, we note the Committee's deliberations regarding utility values used in the economic modelling in section 4.14 of the ACD. On the basis of the available trial evidence, abiraterone does appear to confer important and meaningful QoL benefits, even at an advanced stage of disease. Clearly however, there is considerable uncertainty as to the appropriate values for use in the modelling – and particularly which values adequately reflect the pre- and post-progression health states for patients with metastatic castration-resistant prostate cancer. We note that the Committee felt it inappropriate to rely on evidence from different sources for the purposes of modelling utilities for patients in the pre- and post-progression health states. Whilst the advantages of using evidence from a single source are obvious, it is surely not uncommon to have to draw on a variety of sources and this is often simply a reflection of the limitations of clinical trials.

Finally, we note that in section 4.19 of the ACD, the Committee rejects the idea that abiraterone is licensed for a small patient population and reaches a view that it does not meet the so-called end-of-life criteria. This view appears contrary to the view of the Evidence Review Group and, perhaps more significantly, is inconsistent with decisions made by NICE for other technologies. Full details of the Committee's reasoning in this instance are not provided.

However, the ACD quotes the manufacturer's estimate that approximately 4,300 people with metastatic castration-resistant prostate cancer were receiving docetaxel in England and Wales in 2011, and that approximately 75% of these (3,300) would be eligible for abiraterone. Even assuming 100% of these patients were eligible for treatment with abiraterone (i.e. 4,300), the numbers involved would be significantly smaller than for other technologies that NICE has previously determined do meet the end-of-life criteria. For example in its appraisal of trastuzumab for gastric cancer (TA 208), the Appraisal Committee

considered that 7,000 was "at the upper end of the population size for which it understood the supplementary advice to apply."

In view of these comments, the ICR would urge NICE to reconsider its draft recommendations for abiraterone. Specifically, and given the major advance in treatment outcomes that abiraterone offers, it is important that the Committee re-considers whether a subgroup of patients could be considered cost-effective. On the basis of the Evidence Review Group's assessment of ICERs for the 1 prior chemotherapy group, it seems this might well be the case – particularly since it does appear to us that the end-of-life criteria should apply in this instance.

We are happy to amplify on or clarify these comments if that would be helpful to the NICE's work regarding abiraterone. Meanwhile, we urge NICE to look at all possible avenues to allow some use of this therapy on the NHS in groups that might benefit from it.

Yours sincerely