# NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

## Single Technology Appraisal (STA)

Abiraterone for the treatment of metastatic castration resistant prostate cancer following previous cytotoxic therapy

Thank you for agreeing to give us a statement on your organisation's view of the technology and the way it should be used in the NHS.

Healthcare professionals can provide a unique perspective on the technology within the context of current clinical practice which is not typically available from the published literature.

To help you in making your statement, we have provided a template. The questions are there as prompts to guide you. It is not essential that you answer all of them.

Please do not exceed the 8-page limit.

**About you**
**Your name:** [redacted]**:**

**Name of your organisation:**

**NCRI/RCP/RCR/ACP/JCCO**

**Comments coordinated by:** [redacted]

**Are you (tick all that apply):**

- a specialist in the treatment of people with the condition for which NICE is considering this technology? Yes
- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)? Yes
- an employee of a healthcare professional organisation that represents clinicians treating the condition for which NICE is considering the technology? If so, what is your position in the organisation where appropriate (e.g. policy officer, trustee, member etc.)? Dr Staffurth is a member of the Prostate Clinical Studies Group of the NCRI, a Fellow of both the RCP and RCR. Dr Syndikus is a member of the Prostate Clinical Studies Group of the NCRI, a Fellow of both the RCP and RCR.
- other? (please specify)

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**What is the expected place of the technology in current practice?**

How is the condition currently treated in the NHS? Is there significant geographical variation in current practice? Are there differences of opinion between professionals as to what current practice should be? What are the current alternatives (if any) to the technology, and what are their respective advantages and disadvantages?

Are there any subgroups of patients with the condition who have a different prognosis from the typical patient? Are there differences in the capacity of different subgroups to benefit from or to be put at risk by the technology?

In what setting should/could the technology be used – for example, primary or secondary care, specialist clinics? Would there be any requirements for additional professional input (for example, community care, specialist nursing, other healthcare professionals)?

If the technology is already available, is there variation in how it is being used in the NHS? Is it always used within its licensed indications? If not, under what circumstances does this occur?

Please tell us about any relevant **clinical guidelines** and comment on the appropriateness of the methodology used in developing the guideline and the specific evidence that underpinned the various recommendations.

The NICE guideline prostate: diagnosis and treatment 2008 outlines the general management policies for patients with hormone refractory prostate cancer. We believe that this practice is standardised across UK. The goal of the treatment is to improve survival and control symptoms effectively.
Patients are managed jointly by urologists or oncologists (clinical or medical) with a special interest in urological malignancies within a multi-disciplinary setting, the palliative care team and the general practitioner.
At relapse, second or third line hormone therapy with an antiandrogen (usually bicalutamide, steroids or stilboestrol) is added. Response rates are low (20-30%) and often short lived. Once patients progress after second line hormone therapy and they are fit for intensive chemotherapy, they are managed by oncologists. The next of line of therapy is docetaxel, which has been shown to provide a survival advantage – see Technology Appraisal No. 101, Jun 2006, 'Docetaxel for the treatment of hormone refractory prostate cancer'.
If patients progress after docetaxel chemotherapy (or after an additional second line chemotherapy treatment), many are not fit for more chemotherapy and they are often very symptomatic with bone pain and a general decline in performance status together with urinary symptoms from progressive local disease in the pelvis. Bone targeted therapies (palliative radiotherapy, strontium, bisphosphonates) are used in conjunction with analgesics to control bone pain. Obstructive uropathy, haematuria, lower urinary tract outflow obstruction, lymph oedema and bowel obstruction are managed with a combination of nephrostomies or stents, surgery and urinary

catheters and palliative radiotherapy. The management requires individual assessment and multidisciplinary management; many patients require several interventions as disease progression is often slow, but symptom relief is either not effective in the longer term or new symptoms arise. Interventions vary according to the patient's symptoms and wishes, but also depend on the clinicians' experience, local drug policies and access to palliative care and oncology services. Because none of these therapies has shown any survival benefit and effectiveness is limited, regional variations do exist but are difficult to quantify.

Abiraterone acetate with prednisolone has been shown to provide advantage in this group of patients compared to prednisolone and placebo. Cabazitaxel has also been shown to improve survival in a Phase III trial in a similar group of patients who have progressed despite docetaxel chemotherapy. It should be noted that not all patients within the COU-AA-301 trial would have been considered fit enough to consider enrolment in the cabazitaxel trial (TROPIC) as they would have been fit enough for second-line chemotherapy. Abiraterone should therefore not be directly compared with cabazitaxel. In addition, there is a difference in the comparator arm for the two trials (TROPIC and COU-AA-301) i.e. placebo in the case of abiraterone and mitoxantrone in the case of cabazitaxel. A press release has also suggested an improvement in survival with a novel radio-isotope – alpharadin in patients who were not due to receive docetaxel chemotherapy for at least six months (i.e. had received it already, were not fit enough or did not want chemotherapy).
Currently the experience with the 3 new agents is still very limited. Abiraterone has a favourable toxicity profile compared to second line chemotherapy and will be the drug of choice for patients who are not fit for more chemotherapy. It is also particularly suitable for patients with extensive soft tissue disease. Alpharadin will be a treatment of choice for patients who have not received docetaxel chemotherapy and have troublesome bone pain. With more experience, these drugs will be used consecutively and fit patients might benefit from several lines of treatment.

Abiraterone is licensed in the US, Canada and has just received its European license. It would be used by oncologists who specialise in treating prostate cancer and will be an option of treatment for patients with metastatic prostate cancer whose disease shows progression despite docetaxel chemotherapy.

There is as yet no clear indication from the pivotal COU-AA-301 trial of a subgroup of patients who do not benefit abiraterone.

We believe that abiraterone should only be prescribed within secondary care by medical or clinical oncologists with a special interest in urological malignancies. Present access to abiraterone is extremely limited. There are no relevant guidelines.

There is a second ongoing phase III clinical trial COU-AA-302, in which the use of abiraterone prior to docetaxel chemotherapy is being investigated. It has closed for recruitment, but no efficacy data has yet been released, presented or published.

Abiraterone may have a role in combination with initial hormonal therapy and is expected to be introduced into the ongoing MRC STAMPEDE study shortly.

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**The advantages and disadvantages of the technology**

NICE is particularly interested in your views on how the technology, when it becomes available, will compare with current alternatives used in the UK. Will the technology be easier or more difficult to use, and are there any practical implications (for example, concomitant treatments, other additional clinical requirements, patient acceptability/ease of use or the need for additional tests) surrounding its future use?

If appropriate, please give your view on the nature of any rules, informal or formal, for starting and stopping the use of the technology; this might include any requirements for additional testing to identify appropriate subgroups for treatment or to assess response and the potential for discontinuation.

If you are familiar with the evidence base for the technology, please comment on whether the use of the technology under clinical trial conditions reflects that observed in clinical practice. Do the circumstances in which the trials were conducted reflect current UK practice, and if not, how could the results be extrapolated to a UK setting? What, in your view, are the most important outcomes, and were they measured in the trials? If surrogate measures of outcome were used, do they adequately predict long-term outcomes?

What is the relative significance of any side effects or adverse reactions? In what ways do these affect the management of the condition and the patient's quality of life? Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently during routine clinical practice?

Abiraterone acetate should be considered to be primarily an additional treatment option for men with castrate-refractory post-docetaxel metastatic prostate cancer. The pivotal COA-AA-301 trial has shown an improvement in overall survival in the initial paper of 3.9 months with abiraterone plus prednisolone compared to the standard therapy of prednisolone only. We believe from the experience of patients treated in the Cougar trials, that abiraterone not only improves survival, but also very effectively controls symptoms and reduces skeletal related events. We believe it will reduce the resources required to look after these patients because of better symptom control. There are no specific tests that will be used in routine clinical practice to ascertain suitability for abiraterone.

Abiraterone is a well tolerated oral medication taken once daily. We believe that 3 months of treatment should be employed as a minimum before treatment-failure is defined (unless there is marked clinical deterioration). There is at yet no routine test to identify subgroups likely to benefit more or less than the group as a whole. We believe that patients recruited into COU-AA-301 broadly represent this patient group; outside the trial, doctors might feel that patients with a less favourable performance status would also potentially benefit.

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The trial required patients to maintain on drug until PSA, clinical and radiological progression. We believe that patients may discontinue therapy earlier (based on PSA and clinical progression alone) in the real setting of the NHS in the UK. From our limited personal experience, disease progression seems often rapid once abiraterone was stopped and patients entered the terminal phase of their illness shortly afterwards. The drug access is still very limited and most clinicians have treated only a few patients with abiraterone. The drug has become available since March 2011 with an early access program and since September 2011 access is facilitated by the High Cost Cancer Drug Fund.

The acute side effects are manageable and related to disturbance of the mineralocorticoid pathway. Regular monitoring of liver function tests, potassium levels and blood pressure every 2 weeks initially is currently mandatory and should be provided by an clinician with experience in managing metastatic hormone relapsed prostate cancer.

**Any additional sources of evidence**

Can you provide information about any relevant evidence that might not be found by a technology-focused systematic review of the available trial evidence? This could be information on recent and informal unpublished evidence, or information from registries and other nationally coordinated clinical audits. Any such information must include sufficient detail to allow a judgement to be made as to the quality of the evidence and to allow potential sources of bias to be determined.

The access to abiraterone has been very limited and hence there is no additional information outside the trial available yet. An updated survival analysis will be presented on COU-AA-301 at ECCO 2011 Lead author Dr Fizazi.

Patients' functional status during the COU-AA-301 trial have been submitted to ECCO 2011 Lead author Dr Harland.

British Uro-oncology Group conducted a survey of specialist oncologists who treat prostate cancer to look at their views regarding the forthcoming developments in systemic therapy of prostate cancer. This has been submitted for publication to BJUI.

**Implementation issues**

The NHS is required by the Department of Health and the Welsh Assembly Government to provide funding and resources for medicines and treatments that have been recommended by NICE technology appraisal guidance. This provision has to be made within 3 months from the date of publication of the guidance.

If the technology is unlikely to be available in sufficient quantity, or the staff and facilities to fulfil the general nature of the guidance cannot be put in place within

3 months, NICE may advise the Department of Health and the Welsh Assembly Government to vary this direction.

Please note that NICE cannot suggest such a variation on the basis of budgetary constraints alone.

How would possible NICE guidance on this technology affect the delivery of care for patients with this condition? Would NHS staff need extra education and training? Would any additional resources be required (for example, facilities or equipment)?

There are no additional resources required as the drug is easy to deliver and toxicities are easy to manage; the toxicity profile is favourable compared to second line chemotherapy. The only concern is the increased frequency of assessment during the initial stages of treatment initiations (2 weekly), but these patients are already seen very regularly (6 weekly) in clinics and would require less interventions as they have better symptom control.

**Equality**

Are there any issues that require special attention in light of the NICE's duties to have due regard to the need to eliminate unlawful discrimination and promote equality and foster good relations between people with a characteristic protected by the equalities legislation and others?

No, as yet there are no patients that can be identified who have a better or worse outcome