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: British Uro-Oncology Group

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.)Yes both members of the British Uro-Oncology Group
- 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.

Metastatic prostate cancer is managed by urologists or oncologists (clinical or medical) with a special interest in urological malignancies within a multi-disciplinary setting. Patients are treated initially with androgen deprivation therapy (medical or surgical castration) and at relapse have an antiandrogen added. When patients progress after these two lines of therapies, they are usually all managed by oncologists as the next of line of therapy is often docetaxel or further hormone manipulation such as with an oral oestrogen or steroid depending on disease and patient features of progression. Docetaxel has been shown to provide a survival advantage for men with hormone refractory metastatic prostate cancer– see Technology Appraisal No. 101, Jun 2006, 'Docetaxel for the treatment of hormone refractory prostate cancer'. We believe that this practice is highly standardised across UK.

There is no NICE approved treatment which offers a survival benefit in patients who have progressed after docetaxel chemotherapy. Abiraterone acetate with prednisolone has been shown to provide an 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 (but not identical) group of patients who have progressed despite docetaxel chemotherapy. A press release has suggested an improvement in survival with a novel radio-isotope – alpharadin in a similar (but not identical) group of patients.

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Standard management of these patients at present palliative in nature and is individualised based on their pattern of disease, performance status, co-morbid conditions and individual patient wishes. Treatment options over and above best supportive care (including palliative care) include 2nd line chemotherapy, additional hormonal agents, external beam radiotherapy, radioisotopes, bisphosphonates and clinical trials.

Abiraterone is licensed in the US, Canada and has just received its European and UK 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.

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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. In an updated analysis (with follow-up period of 20.2 months) results were consistent, showing 4.6 month improvement in median overall survival benefit for abiraterone acetate and prednisolone compared with placebo and prednisolone, (15.8 months vs 11.2 months) 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 therapy 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-30 broadly represent this patient group.

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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.

The acute side effects are minimal and related to disturbance of the mineralocorticoid pathway. Monitoring of liver function tests, potassium levels and blood pressure is advisable.

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.

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.

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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)?

Minimally as the drug is easy to deliver and toxicities are easy to manage
These patients are already seen very regularly in clinics

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