Appendix G - professional organisation submission template

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Enzalutamide for treating metastatic hormone-relapsed prostate cancer not previously treated with chemotherapy

Thank you for agreeing to make a submission 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 submission, 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 Association of Urological Surgeons (BAUS)
Are you (tick all that apply):

- a specialist in the treatment of people with the condition for which NICE is considering this technology?
- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)?
- 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)?
- 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?

The condition is currently treated with Docetaxel chemotherapy or Abiraterone/prednisolone if the patient is suitable from a medical viewpoint. If not, maximal androgen blockade is continued with the addition of dexamethasone or diethylstilboestrol. The condition is often found in elderly patients who cannot tolerate these alternatives, particularly chemotherapy. All the alternatives to Enzalutamide are potentially more toxic: Docetaxel chemotherapy can cause neutropenic sepsis (5%), rarely fatal; Abiraterone/prednisolone can cause cardiac failure, liver dysfunction / hypertension and electrolyte disturbances; diethylstilboestrol can cause venous thrombo-embolism. Enzalutamide is a safe drug whose main side effect is hypertension, managed easily with medical means, the only contra-indication being a history of convulsions.

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?

Patients who are fit for cytotoxic chemotherapy with symptomatic metastatic disease burden should be treated with Docetaxel if fit enough, since the clinical trials of abiraterone and enzalutamide did not include such patients.

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)?

Enzalutamide should be used in secondary care under the supervision of an appropriate specialist (either urologist or oncologist) with the approval of the urology MDT where possible

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?

Enzalutamide is currently used for patients with castrate-resistant prostate cancer (CRPC), either before or after Docetaxel chemotherapy (both its licensed indications). It is used exclusively by oncologists under current prescribing arrangements.

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.

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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?

Patients often remain under the care of a urologist when being treated with androgen deprivation therapy for advanced prostate cancer. At the time of disease relapse, we feel that Enzalutamide will be easier for urologists to use, in conjunction with the MDT approval, on appropriate patients compared with the current alternatives. It is orally-administered and generally safe. This may reduce the waiting time (for patients to see an oncologist) before starting this treatment, or indeed may obviate the need for patients to see an oncologist at that stage in their disease. We are also aware that many patients do not have easy access to specialist oncology, particularly in peripheral hospitals where oncology input is of a general nature. We believe that patients will be deprived of their proper treatment options if urologists are not able to prescribe this medication.

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.

BAUS would suggest that patients with heavy symptomatic castrate resistant disease who are fit for cytotoxic chemotherapy should be considered for treatment with either Docetaxel based chemotherapy or novel androgenic agents, Abiraterone / Steroid or Enzalutamide. Those who are not considered fit enough for cytotoxic chemotherapy should be treated with enzalutiamide or abiraterone and steroid. Novel anti-androgenic treatment should be continued for a minimum of 3 months (provided the side effect profile is acceptable) in order to assess therapeutic response.

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?

The PREVAIL trial (Beer TM et al, NEJM 2014, 371; 424-433) was conducted in previously-untreated CRPC patients with asymptomatic or mildly symptomatic bone and/or visceral metastases. This is typical of current UK practice. The most important findings of the PREVAIL trial were that Enzalutamide delayed time to chemotherapy by 17 months and

prolonged overall survival by > 2 months compared with placebo. These are important outcome advantages for patients.

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?

Enzalutamide is widely regarded as a safe drug with rare serious adverse events in clinical trials. The most common significant side effect is hypertension, which is easily managed using standard therapies. We are not aware of any adverse effects that were not apparent in clinical trials but have come to light subsequently during routine clinical practice.

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.

None provided

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)?

NICE guidance on Enzalutamide relating to CRPC patients in the pre-chemotherapy setting would be good for these patients, who are usually referred back to their urologist by primary care, especially those with mild symptoms who were unsuitable for Docetaxel chemotherapy.

It would not require NHS staff education and training, nor additional resources for facilities and equipment.

Equality

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that this appraisal:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which [the treatment(s)] is/are/will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could lead to recommendations that have any adverse impact on people with a particular disability or disabilities.

No issues

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

No issues