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 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?
- √ 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)? **Chair: British Uro-oncology Group**
- other? (please specify)

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Single Technology Appraisal (STA)

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

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

Men with metastatic Castration Resistant Prostate Cancer (mCRPC), whose disease is asymptomatic or mildly symptomatic, and for whom chemotherapy may not be immediately appropriate or necessary, have limited treatment options. The British Uro-oncology Group welcomes enzalutamide as a clinically significant therapeutic option in this setting. It has the potential to prolong survival, palliate symptoms, and improve quality of life for a large number of such men.

The advantages and disadvantages of the technology

Enzalutamide met both its primary endpoints of overall survival (OS) and radiographic progression free survival (rPFS) in the PREVAIL study. The PREVAIL results were reviewed by the independent Data Monitoring Committee after 540 deaths and in light of statistically significant benefits in OS and rPFS in favour of enzalutamide, the PREVAIL trial was stopped and unblinded. The time on the study drug was more than three times longer for enzalutamide than placebo with a median treatment duration of 16.6 months versus 4.6 months. At the time of the data cut-off 42.1% of men continued on enzalutamide versus only 7.2% of the placebo group continuing.

At the point of analysis, 72% of patients in the enzalutamide group were alive, compared to 63% in the placebo group (HR, 0.71; 95% CI, 0.60 to 0.84; P<0.001). Enzalutamide reduced the risk of death by 29%. This survival benefit was reported across all subgroups including those with European Co-operative Group (ECOG) performance status 0 or 1, ages above or below 75, different geographical locations and those men with or without visceral disease. A significant difference in the rate of rPFS was also reported, with no progression in 65% of subjects in the enzalutamide group compared to 14% in the placebo group (HR, 0.19; 95% CI, 0.15 to 0.23; P<0.001). This 81% reduction in the risk of radiographic progression is both statistically and clinically significant, and applies to all subgroups including those with visceral metastases.

Enzalutamdie also showed benefits with regard to secondary endpoints, which are of critical importance for patients. Other treatments in this setting have shown tumour activity and this will often improve quality of life (QOL) by reducing the cancer disease burden and consequently the complications of prostate cancer. However there is a balance between this efficacy and the tolerability and ease of access to drugs which is important to maintain the optimal quality of life for our patients.

In the PREVAIL study, there was a significant delay in the time to QOL deterioration as measured by the validated FACT-P scoring tool. The time to FACT-P global score decline was 11.3 months for enzalutamide and 5.6 months for placebo patients respectively (HR, 0.169; p<0.0001). Enzalutamide also significantly delayed the median time to cytotoxic chemotherapy by 17 months. A 28 month delay was seen in enzalutamide patients compared to 10.8 months for placebo (HR, 0.35 95% CI: 0.30–0.40; p<0.0001. Other secondary endpoints which showed significant benefit for enzalutamide included the time to first

skeletal-related event (HR, 0.72), time to PSA progression (HR, 0.17), and the number of subjects experiencing a PSA drop of at least 50% (78% vs. 3%) (P<0.001 for all comparisons).

The excellent tolerability of enzalutamide previously demonstrated in the earlier AFFIRM study was confirmed in the PREVAIL study. Adverse events were similar in both arms of the trial and reported for 96.9% of men receiving enzalutamide and 93.2% for placebo. It is important to note the difference in duration of study drug which was longer for enzalutamide (16.6 vs 4.6 months for placebo). Study discontinuation due to an adverse event occurred in 5.6% of the enzalutamide group and 6.0% of placebo patients.

The most common clinically relevant adverse events associated with enzalutamide were fatigue (35.6% vs 25.8%) and hypertension (13.4% vs 4.1%). There was a very low risk of abnormalities in liver function tests in both groups (0.9% vs 0.6%) with no need for routine monitoring of patients on enzalutamide. There was no increase in the seizure risk with one seizure reported in the placebo group during the monitoring period and one seizure in the enzalutamide group after the data cut-off period.

In summary, enzalutamide demonstrates excellent efficacy and tolerability with meaningful endpoints and maintenance of QOL for men with mCRPC.

Implementation issues

As a tablet form enzalutamide can be dispensed immediately and no implementation issues are envisaged.

There is no need for concomitant steroids with their attendant toxicities. There is no additional monitoring nor additional out patient monitoring which reduces the need for patients to make additional visits to clinic and have additional blood tests. There is also no need for fasting.

In the UK, responsibility for initiating treatment and managing patients will most likely lie with the oncologist and their team. [BJU Int 2012 Sep;110(5):658-67] Service systems are continuously evolving, particularly in the rapidly changing field of prostate cancer, to accommodate the introduction of new treatments to improve patient outcomes.

Equality

There should not be any issues relating to equality of patients as they would be under the care of the clinical/medical oncologist.

The British Uro-oncology Group strongly supports a positive NICE appraisal allowing NHS prescribing of enzalutamide in chemotherapy naive patients. The addition of enzalutamide at progression, provides meaningful clinical benefit to men with metastatic castration resistant prostate cancer and it is very well tolerated, providing patients with optimal quality of life.