HEALTH TECHNOLOGY APPRAISAL: Docetaxel for the treatment of hormone-refractory metastatic prostate cancer. Comment on: Appraisal Consultation Document (ACD)	
To: NICE	**FROM: NHS Quality Improvement Scotland**

Reviewer 1.

1. **Whether you consider that all the relevant evidence has been taken into account.**

Yes

2. **Whether you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence and that the preliminary views on the resource impact and implications for the NHS are appropriate.**

Yes

3. **Whether you consider that the provisional recommendations of the Appraisal Committee are sound and constitute a suitable basis for the preparation of guidance to the NHS.**

Yes

Reviewer 2.

1. I did enjoy reading the documents and was very impressed. They are clear and well-reasoned and I did not have cause to disagree with any of the recommendations.
They recommend docetaxel as a treatment option for patients who are asymptomatic and have only laboratory or radiological evidence of progression. This group of patients were also included in the TAX 327 study and so the evidence base is there. Where chemotherapy is palliative some consultants advise using it in patients with symptoms from their disease and not necessarily using it in patients who are asymptomatic and whose quality of life is already good. The guidance, by calling it a treatment option does allow for treatment to be given immediately when there is biochemical evidence of progressive disease or deferred until symptoms develop.
In relation to my clinical practice the guidelines are extremely welcome because at present use of docetaxel is not permitted for prostate cancer but I may use mitoxantrone

(outside its licence). It is clear that for most patients docetaxel has superior efficacy and I have been very keen to use it in selected patients with good performance status especially those with symptoms.

2. This is as usual a comprehensive review of the limited available literature, but it does rely very heavily on a single randomised trial. This did show advantages for docetaxel, but the advantage in median survival, while statistically significant, was only 2.4 months. There were benefits in quality of life and pain too, but a significantly greater risk of major adverse events which were more likely to be associated with longer term morbidity. Although described as 'cost-effective' the figures provided by the company and the assessment group are at the upper limit of usual acceptability and exceed £30k. In the absence of any effective treatment for this condition there will be very considerable pressure to make even a marginally effective treatment available, but this ACD does not seem to follow its own logic in the conclusions reached. A conclusion that docetaxel is marginally effective, toxic and expensive would seem to be equally supported by the evidence reviewed.

Additional supporting evidence would seem to be necessary if the conclusion of the ACD is to be the outcome of the FAD in due course.

Reviewer 3.

OVERVIEW - Issues for consideration

1. How generalisable are the results of TAX327? This issue has been raised in section 3.1 Clinical effectiveness.

I believe they are, for appropriate groups

2 How relevant to this appraisal for docetaxel in combination with prednisolone are trials investigating docetaxel in combination with estramustine and/or prednisone? This issue has been raised in section 3.1 Clinical effectiveness.

Difficult to advise. Probably best ignored

*3.*What is the clinical significance of the results? The Assessment Report states that while pain reduction and improvements in quality of life were achieved in substantial proportions of patients prior to the licensing of docetaxel for the treatment of mHRPC, survival did not appear to be prolonged. The sponsor submission states that docetaxel is unique in that it significantly extends life in patients with mHRPC, in addition to providing palliative benefits.

Survival issue is important – only treatment shown to improve survival in this group of patients, and will form the basis for future research trials

a. Can the evidence available inform the identification of subgroups for which the intervention would be particularly clinically effective or cost effective? All of the trials reviewed required patients to be of a minimum performance status in order to be recruited. TAX327, Oudard and SWOG

9916 stratified patients according to performance status (but by a different scale of measurement in each). It has been suggested in a consultee submission that the intervention could be considered after disease progression following at least two hormonal manipulations.

Suggested requirements reasonable. Intervention should be considered after failure to respond to hormones – number of agents irrelevant. If a patient consistently shows responses to hormone manoeuvres, Docetaxel would not be appropriate till they stop. If they fail to respond to first line hormone, further hormone treatments are a waste of time.

b. The role of steroids in combination with chemotherapy should be considered when discussing the clinical evidence. It is unclear how the selection (for example, dexamethasone or prednisolone), dosage and administration of premedication may have impacted on the clinical evidence.

Can't say, but little effect. Ignore

c. Questions remain about how many cycles of docetaxel should optimally be given. This issue has been raised in section 3.2 Cost effectiveness, and discussion of this point may be of value.

Depends on response. For most patients in UK, will probably receive maximum of 6 cycles, but will depend on clinical situation and response. The use of 10 cycles in the TAX 327 trial had more to do with Mitoxantrone use, particularly in US practice