

National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

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

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

Comment 1: the draft remit

Section	Consultees	Comments	Action
Appropriateness	Astellas Pharma	Yes	Comment noted.
	Prostate Cancer Support Federation	Yes	Comment noted.
	Prostate Cancer UK	It would be appropriate to refer this topic to NICE for appraisal. Treatment options for men with metastatic hormone-relapsed prostate cancer are limited and it would be desirable to increase the range of effective treatments available for these patients, particularly if this leads to extended overall and progression-free survival. Should the proposed appraisal recommend that enzalutamide is effective for the above indication, it will help to provide standardised access and increased treatment choice to a group of patients who currently have a restricted range of treatments available once their cancer becomes castration-resistant.	Comment noted.
Wording	Astellas Pharma	Yes	Comment noted. The remit has been updated in line with the discussions at the scoping workshop to reflect that enzalutamide is being considered for people in whom chemotherapy is not yet clinically indicated.

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	Prostate Cancer Support Federation	The wording should take into account that at present there is no treatment pathway that includes bone health with either bisphosphonates or denosumab for advanced prostate cancer. As it has been proven that these new drugs extend life so successfully that compression does become a problem, this is something that should be included in the wording.	Comment noted. The wording of the remit only reflects the main objective of the appraisal, rather than specific issues to be considered during the appraisal. In addition the discussion on bone health treatment pathway is outside the remit for this topic.
Timing Issues	Astellas Pharma	There is currently no NICE recommended alternative to docetaxel for the treatment of hormone relapsed metastatic prostate cancer.	Comment noted. The remit has been updated in line with the discussions at the scoping workshop to reflect that enzalutamide is being considered for people in whom chemotherapy is not yet clinically indicated. Therefore docetaxel is not considered a comparator for enzalutamide because it would be used later in the pathway.
	British Association of Urology Nurses	Potentially urgent due to Enzalutamide currently being unavailable to post Abiraterone patients following closure of the compassionate use program	Comment noted. NICE aims to provide draft guidance to the NHS within 6 months from the date when the marketing authorisation for a technology is granted.
	Prostate Cancer Support Federation	Very urgent, results show a much better outcome if it is used before chemotherapy. It is also good for the patient not to have to go through the trauma of chemotherapy	Comments noted. NICE aims to provide draft guidance to the NHS within 6 months from the date when the marketing authorisation for a technology is granted.
	Prostate Cancer UK	Prostate Cancer UK welcomes NICE's proposed Single Technology Appraisal of enzalutamide for this indication. Should the proposed appraisal recommend that this agent is effective, it will help to provide standardised access and increased patient choice to these patients.	Comment noted.

Comment 2: the draft scope

Section	Consultees	Comments	Action
Background information	Prostate Cancer Support Federation	All correct to my knowledge	Comment noted.
The technology/ intervention	Astellas Pharma	In this section the following information can now be included: The phase 3 PREVAIL study has been stopped following a review by the Independent Data Monitoring Committee (IDMC) of a planned interim data analysis. This is due to observed benefits in the study's co-primary endpoints of overall survival and radiographic progression free survival, and the observed safety profile. The IDMC recommended the study be stopped and patients treated with placebo be offered enzalutamide.	Comment noted. Specific details of the clinical trials are not usually included in the scope.
	British Association of Urology Nurses	Yes	Comment noted.
	Prostate Cancer Support Federation	All correct to my knowledge	Comment noted.
	Prostate Cancer UK	Yes	Comment noted.
Population	Astellas Pharma	Population appropriately defined. Not aware of any subgroups that should be treated separately.	Comment noted. The population has been updated in line with the discussions at the scoping workshop to reflect that enzalutamide is being considered for people in whom chemotherapy is not yet clinically indicated.

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	British Association of Urology Nurses	Yes	Comment noted. The population has been updated in line with the discussions at the scoping workshop to reflect that enzalutamide is being considered for people in whom chemotherapy is not yet clinically indicated.
	Prostate Cancer Support Federation	All correct to my knowledge	Comment noted. The population has been updated in line with the discussions at the scoping workshop to reflect that enzalutamide is being considered for people in whom chemotherapy is not yet clinically indicated.
	Prostate Cancer UK	Prostate Cancer UK believes this population has been correctly defined.	Comment noted. The population has been updated in line with the discussions at the scoping workshop to reflect that enzalutamide is being considered for people in whom chemotherapy is not yet clinically indicated.

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Comparators	Astellas Pharma	<p>Abiraterone, docetaxel and best supportive care are all currently used in the NHS. Abiraterone, due to the absence of a NICE appraisal, can only be accessed in England via the Cancer Drugs Fund, and so is not available in Wales.</p> <p>If the STA for abiraterone remains suspended, will it still be a relevant comparator?</p> <p>If the STA for abiraterone goes ahead and it is not recommended by NICE will it still be a relevant comparator?</p> <p>Best supportive care is most likely to be used in patients who are unable to access abiraterone, and who are not suitable/well enough to receive docetaxel.</p>	<p>Comments noted. The comparators have been updated to best supportive care and abiraterone (in combination with prednisone or prednisolone) in line with the discussions at the scoping workshop. Docetaxel has been removed from the comparators because it is used later in the treatment pathway.</p> <p>Technologies without NICE guidance, or not recommended by NICE, can be considered as relevant comparators, if they are widely used in clinical practice, including those available through the Cancer Drugs Fund. NICE develops guidance for England.</p>

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	British Association of Urology Nurses	<p>Not comparable with 'Best Supportive Care' as this relates to "Treatment administered with the intent to maximise Quality of Life without a specific anti neoplastic regimen"</p> <p>Suggest that Diethylstilboestrol plus aspirin and steroids (Prednisolone, Dexamethasone) alone are added to the comparators, as these were standard care before Abiraterone and Enzalutamide. And, of course will remain so for patients who do not fulfil the criteria for these new drugs.</p>	<p>Comments noted. The comparators have been updated to best supportive care and abiraterone (in combination with prednisone or prednisolone) in line with the discussions at the scoping workshop.</p> <p>The workshop attendees indicated that dexamethasone and prednisolone were considered as best supportive care.</p>
	Prostate Cancer Support Federation	All correct to my knowledge	<p>Comments noted. However, the comparators have been updated to best supportive care and abiraterone (in combination with prednisone or prednisolone) in line with the discussions at the scoping workshop. Docetaxel has been removed from the comparators because it is used later in the treatment pathway.</p>

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	Prostate Cancer UK	The correct comparators are identified.	Comments noted. However, the comparators have been updated to best supportive care and abiraterone (in combination with prednisone or prednisolone) in line with the discussions at the scoping workshop. Docetaxel has been removed from the comparators because it is used later in the treatment pathway.
Outcomes	Astellas Pharma	Need to include radiographic progression free survival	Comment noted. The scope has been updated to include radiographic progression-free survival and also time to initiation of cytotoxic chemotherapy in line with the discussions at the scoping workshop.
	British Association of Urology Nurses	Yes	Comment noted. The scope has been updated to include radiographic progression-free survival and also time to initiation of cytotoxic chemotherapy in line with the discussions at the scoping workshop.

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	Prostate Cancer Support Federation	Yes to my knowledge	Comment noted. The scope has been updated to include radiographic progression-free survival and also time to initiation of cytotoxic chemotherapy in line with the discussions at the scoping workshop.
	Prostate Cancer UK	<p>The relevant clinical outcomes we would identify are those already set out in the draft scope. However, it is important that health-related quality of life and adverse effects are considered with an equal standing to the other outcomes. Patient-reported outcomes should also be considered, to ensure that the agent is not only clinically effective but also improves outcomes of importance to this patient population.</p> <p>Health-related quality of life is particularly crucial at this point in the cancer journey for a man with castrate resistant disease. Aspects that relate to quality of life should be specifically considered, including the impact of the treatment regimen on number of hospital appointments, method of delivering treatment (e.g. oral, intravenous etc.) and side effects.</p>	Comment noted. The Appraisal Committee makes recommendations using all available evidence provided.
Economic analysis	Prostate Cancer Support Federation	Sooner the better	Comment noted.
	Prostate Cancer UK	We do not have enough evidence to enable us to comment on this area.	Comment noted.

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Equality and Diversity	Prostate Cancer Support Federation	<p>The only equality issue is that there is no bone health treatment pathway for prostate cancer as there is for breast and other cancers. This amounts to sexual discrimination.</p> <p>This is even more important now that life prolonging drugs are being given and statistics prove that spinal compression, although rare in prostate cancer, is becoming an increasing problem now that men are living longer.</p>	<p>This is not an issue specific to enzalutamide, and therefore cannot be addressed in this STA.</p> <p>In general, recommendations for one technology can differ between diseases (where one predominantly affects women and the other predominantly affects men), and this in itself cannot be regarded as sex discrimination. Such differences could have been as a result of the evidence available which could have led to a particular technology being more clinically or cost-effective in one disease area than another, or in one population group than another.</p> <p>As far as enzalutamide is concerned, if evidence on the effect of enzalutamide on bone health is available, this will be fully considered in the appraisal.</p>

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	Prostate Cancer UK	<p>It will be important to ensure that access to this technology is equitable and discrimination does not occur solely on the basis of age, ethnicity or socio-economic status. Prostate cancer is more common in men aged over 60 and African Caribbean men are three times more likely to develop prostate cancer than white men of the same age in the UK. Furthermore, men from lower socioeconomic backgrounds are less likely to survive prostate cancer than men from more affluent backgrounds. It will be important to ensure that eligible patients from these populations are not denied access to this technology (if approved) because of factors related to their age, ethnicity and socio-economic status. Information and communication strategies must also be considered and patients consulted to ensure that access can be as equitable as possible.</p>	<p>Issues relating to prevalence of a disease or condition between different age, cultural or socio-economic groups cannot be addressed in a NICE technology appraisal guidance.</p> <p>NICE does not intend to restrict access based on age, ethnicity and socio-economic status.</p> <p>.</p>
Innovation	Astellas Pharma	<p>Currently there is no NICE recommended alternative to docetaxel for the treatment of hormone relapsed metastatic prostate cancer.</p> <p>Enzalutamide has advantages over the suggested comparator abiraterone in that it does not require product specific monitoring for liver toxicity and mineralocorticoid excess. Enzalutamide does not need to be administered with corticosteroids as is the case with both docetaxel and abiraterone. Additionally enzalutamide is more convenient for patients to take than abiraterone due to the lack of restriction of taking with food.</p> <p>The recent ACD for enzalutamide in post-chemo hormone relapsed metastatic prostate cancer includes the following statement: 'The Committee agreed that the mechanism of action of enzalutamide is a 'step-change' compared with other androgen receptor blockers</p>	Comment noted.

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	British Association of Urology Nurses	<p>Evidence available which could change the current pathway:</p> <p>Evidence that Enzalutamide improves progression-Free Survival in Chemotherapy-Naive Patients With Advanced Prostate Cancer http://investors.medivation.com/releasedetail.cfm?ReleaseID=798880</p> <p>Enzalutamide Plus Abiraterone May Have Higher Response Rate in mCRPC Than Either Agent Alone http://www.onclive.com/conference-coverage/ecco-esmo-2013/Enzalutamide-Plus-Abiraterone-May-Have-Higher-Response-Rate-in-mCRPC-Than-Either-Agent-Alone</p> <p>Papers presented at ESMO conference 2013 suggest pre chemotherapy patients benefit from a 10—20% response to Enzalutamide post Abiraterone and vice versa. Author Johann S. de Bono</p>	Comment noted.
	Prostate Cancer Support Federation	<p>Enzalutamide is a step change in the treatment of prostate cancer with the potential to not only prolong life, but to allow patients to live a normal life without feeling as though they have advanced prostate cancer. The fact that this could be given before chemotherapy would be an important plus. Chemotherapy is an unpleasant and debilitating experience and the patient would be spared this. Sometimes the effects of chemotherapy last forever (numb toes and broken finger nails etc)</p>	Comment noted.
	Prostate Cancer UK	Yes	Comment noted.

Section	Consultees	Comments	Action
Questions for consultation	Astellas Pharma	<p>Have all relevant comparators for enzalutamide been included in the scope? Yes – see comparator section above.</p> <p>Which treatments are considered to be established clinical practice in the NHS for metastatic hormone-relapsed prostate cancer in people who are asymptomatic or mildly symptomatic? Once patients have relapsed on hormone treatment, the next established treatment option is docetaxel. Individual clinicians will vary in the point at which they introduce docetaxel, with some initiating treatment soon after relapse on hormone treatment, and others waiting for further progression. Some patients may not be treated with docetaxel at all.</p> <p>Is abiraterone routinely used in clinical practice for treating people with metastatic hormone-relapsed prostate cancer who are asymptomatic or mildly symptomatic? In England, but not Wales, abiraterone is used via the Cancer Drugs Fund. Data from the CDF shows variable levels of usage around England, not routine.</p> <p>Is docetaxel a relevant comparator for enzalutamide for this appraisal? Yes, docetaxel is currently the only NICE approved treatment for the indication in this appraisal.</p> <p>How should best supportive care be defined? Is it a relevant comparator for this appraisal? Best supportive care is still a treatment option for patients who are not suitable for docetaxel, and who do not have access to abiraterone. We anticipate that best supportive would include: corticosteroids, pain therapy, radiation therapy, bisphosphonates and LHRH agonists.</p>	<p>Comments noted. The remit and population have been updated in line with the discussions at the scoping workshop to reflect that enzalutamide is being considered for people in whom chemotherapy is not yet clinically indicated. Therefore docetaxel is not considered a comparator for enzalutamide because it would be used later in the pathway.</p> <p>NICE develops guidance for England only.</p>
Additional comments on the draft scope.	Prostate Cancer Support Federation	Look at bone health. Very important!	Comment noted.

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope

Department of Health
Healthcare Improvement Scotland
Royal College of Nursing