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

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Response to consultee and commentator comments on the provisional matrix of consultees and commentators (pre-referral

National Institute for Health and Clinical Excellence

SingleTechnology Appraisal (STA)
Abiraterone for the treatment of metastatic castration-resistant 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	British Uro-oncology Group (BUG)	Yes it is appropriate to review this product now	Comment noted.
	CSAS	This is appropriate	Comment noted.
	Janssen	Janssen believes this is an appropriate topic to refer to NICE for appraisal	Comment noted.
	NHS Bradford and Airedale	This is appropriate	Comment noted.
	The Prostate Cancer Charity	It would be appropriate to refer this topic to NICE for appraisal. Treatment options for men with metastatic castration-resistant 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 abiraterone 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.
	Royal College of Physicians on behalf of NCRI Clinical Studies Group/Royal	yes	Comment noted.

Section	Consultees	Comments	Action
	College of Physicians/Royal College of Radiologists/Joint Collegiate Council on Oncology/Association of Cancer Physicians		
	Sanofi UK	We agree this is an appropriate topic for NICE to appraise.	Comment noted.
Wording	British Uro-oncology Group (BUG)	The pivotal trial was conducted in men who had all received prior docetaxel, but we think this wording is more appropriate for clinical practice	This proposed appraisal relates to an extension of the licence for use in patients not previously treated with chemotherapy. The manufacturer has conducted a trial (NCT00887198) in this population. A separate NICE appraisal has been published for abiraterone following prior chemotherapy (NICE technology appraisal 259).
	CSAS	Yes	Comment noted.
	Janssen	Janssen suggests that the wording of the remit should reflect the anticipated licence as added in italics below: "Abiraterone acetate is indicated for the treatment of metastatic, castration-resistant prostate cancer in men who *are either asymptomatic or mildly symptomatic and* have not been previously treated with chemotherapy	Comment noted. The remit refers to the licensed indications and therefore does not need to be amended.
	NHS Bradford and Airedale	Yes	Comment noted.

Section	Consultees	Comments	Action
	The Prostate Cancer Charity	We would like NICE to reconsider the use of the terms 'castrate-resistant' and 'castration-resistant' prostate cancer, when providing information to patients. Although we acknowledge that these are clinically accurate terms used amongst health professionals, we know that people affected by prostate cancer are generally deterred by them. A recent survey of 27 of the Charity's Prostate Cancer Voices network found that 24 of the respondents said they would prefer to see a different phrase used to describe this type of prostate cancer. 21 respondents said they found the phrase "castration" was an unhelpful way of describing the treatments or type of prostate cancer.	Comment noted. During consultation, clinical experts stated that both 'castration-resistant' and 'castrate-resistant' were used in clinical practice but noted that they are aware of the sensitivity of the term. Consultees agreed that the term used in this appraisal should reflect the marketing authorisation wording and be consistent with other technology appraisal guidance published by NICE. Technology appraisal 259 'Abiraterone for castration resistant metastatic prostate cancer previously treated with a docetaxel-containing regimen' published by NICE in June 2012, uses the term 'castration-resistant'.
	Royal College of Physicians on behalf of NCRI Clinical Studies Group/Royal College of Physicians/Royal College of Radiologists/Joint Collegiate Council on Oncology/Association of Cancer Physicians	yes	Comment noted.

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Timing Issues	British Uro-oncology Group (BUG)	This is an urgent issue as patient's clinical condition changes rapidly and any delays will limit the number of men who may benefit	Comment noted.
	CSAS	Abiraterone does not currently have marketing authorisation in the UK. A phase III RCT was started in April 2009 and is currently ongoing. The estimated final data collection date for the primary outcomes is April 2011 and the study completion date is estimated to be April 2014. No results from this study have yet been published.	Comment noted. NICE aims to produce guidance on the use of new technologies within 6 months from when the marketing authorisation is granted. Appraisals are prioritised to coincide with the timing of marketing authorisation.
	Janssen	Commercial in confidence: [redacted]	Comment noted. NICE notes that CHMP positive opinion for this indication under consideration was granted on 15 Nov 2012.
	NHS Bradford and Airedale	Abiraterone does not currently have marketing authorisation in the UK. A phase III RCT was started in April 2009 and is currently ongoing. The estimated final data collection date for the primary outcomes is April 2011 and the study completion date is estimated to be April 2014. No results from this study have yet been published.	Comment noted. NICE aims to produce guidance on the use of new technologies within 6 months from when the marketing authorisation is granted. Appraisals are prioritised to coincide with the timing of the marketing authorisation.
	The Prostate Cancer Charity	The timing of this appraisal appears appropriate. However it should be noted that treatment options for this patient population are limited. Only docetaxel is licensed for this point in the treatment pathway. The results of the appraisal could improve treatment choice for these patients (should abiraterone be considered effective for this indication) and so should be conducted promptly. Abiraterone has recently been recommended for use in metastatic	Comment noted. NICE aims to produce guidance on the use of new technologies within 6 months from when the marketing authorisation is granted. Appraisals are prioritised to coincide with the timing of the marketing authorisation.

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		castration-resistant prostate cancer by the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP). Market authorisation is therefore likely to occur in the near future and be available for prescribing in England and Wales. It is essential that the appraisal is conducted rapidly, so that appropriate guidance is available for commissioners, clinicians and patients and to ensure equity of access.	
	Royal College of Physicians on behalf of NCRI Clinical Studies Group/Royal College of Physicians/Royal College of Radiologists/Joint Collegiate Council on Oncology/Association of Cancer Physicians	important for men unfit for chemotherapy	Comment noted
Additional comments on the draft remit			

Comment 2: the draft scope

Section	Consultees	Comments	Action
Background information	British Uro-oncology Group (BUG)	Paragraph 4 - Last 2 sentences re management options should note that none have been shown to improve survival. Treatment options should also mention cabzitaxel. This is a chemotherapy that has been shown to improve survival post docetaxel chemotherapy and is licensed in the UK and available via the cancer drugs fund.	Comment noted. This appraisal is concerned with patients who have not received prior chemotherapy. The background of the scope is only intended to provide a brief overview of the disease and its current clinical management. A more thorough description of the clinical aspects of the disease will be considered as part of an appraisal.
	CSAS	This is accurate. The term "Castration refractory prostate cancer" is another alternative name which is used in the relevant National Horizon Scanning Centre 2010 report on abiraterone.	Comment noted.
	Janssen	The statement “The majority of men have histological evidence of prostate cancer by age 80 but are more likely to die of unrelated causes” in the first paragraph appears to be somewhat contradicted by the first sentence of the third paragraph “It is estimated that 55% to 65% of men with prostate cancer will go on to develop metastatic disease.” Janssen believes this statement in the first paragraph underplays the impact that prostate cancer, and in particular metastatic disease, has on the well being and quality of life of these men.	Comment noted. The statement in the first paragraph relates to the prevalence of histological changes in the prostate, which increases with age and in many cases is local and non-metastatic. The sentence has been removed for clarity.
	NHS Bradford and Airedale	This is accurate. The term "Castration refractory prostate cancer" is another alternative name which is used in the relevant National Horizon Scanning Centre 2010 report on abiraterone.	Comment noted. Following the consultation the scope has been amended and now refers to the patient population as

Section	Consultees	Comments	Action
			'castration-resistant'.
	The Prostate Cancer Charity	The Prostate Cancer Charity welcomes the inclusion of information on the number of men with prostate cancer who will go on to develop metastatic disease. This information provides context to assess the need for this technology and the number of patients who may be eligible. Anti-androgens and GnRH antagonists (e.g. degarelix) should be included in the list of standard hormonal treatments for metastatic disease. "Hormone-resistant" should be included in the list of terms which are commonly used to describe prostate cancer that has become resistant to standard hormonal therapy. While the term is not as clinically accurate as the terms already listed in the draft scope, we know that patients prefer "hormone-resistant" rather than the phrase "castration-resistant", as outlined above. It would be helpful to provide a reference for the percentage of men with metastatic prostate cancer who initially respond to hormonal therapy to provide appropriate evidence and context.	Comments noted. The background of the scope is only intended to provide a brief overview of the disease and its current clinical management. The Appraisal Committee will consider the most appropriate comparators and treatment options after assessing advice from clinical experts and the available evidence. During consultation, clinical experts expressed the view that term castration-resistant should be used, rather than hormone resistant, as it reflects the increasing knowledge of the mechanism driving the disease.
	Royal College of Physicians on behalf of NCRI Clinical Studies Group/Royal College of Physicians/Royal College of Radiologists/Joint Collegiate Council on	ok	Comment noted.

Section	Consultees	Comments	Action
	Oncology/Association of Cancer Physicians		
The technology/ intervention	British Uro-oncology Group (BUG)	The trial compared abiraterone and predisone/prednisolone with placebo and prednisone/prednsiolone. The data with abiraterone continues to improve as the data matures. Latest overall survival in the phase 3 trial was 15.8 months in the abiraterone group and 11.2 months in the placebo group (P < .0001); (American Society of Clinical Oncology (ASCO) Meeting 2011).	Comment noted. The Appraisal Committee will consider the evidence from the clinical trial and seek advice from clinical experts when assessing the clinical effectiveness.
	CSAS	Yes	Comment noted.
	Janssen	Janssen suggests that the last sentence of the first paragraph reading: "... It is administered orally." Should be reworded to the following: "...It is administered orally in combination with prednisolone."	Comment noted. The scope has been amended.
	NHS Bradford and Airedale	Yes	Comment noted.
	The Prostate Cancer Charity	Abiraterone has now been recommended for the treatment of metastatic castration-resistant prostate cancer following docetaxel treatment by the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP). Its brand name is Zytiga so the description should be updated to reflect this. It would be helpful to mention the use of abiraterone in the post-chemotherapy indication, its favourable trial result and its licensing, here. It is difficult to comment further on the technology at present as the results of the relevant phase III clinical trial on this indication have not yet been published.	Comments noted. NICE technology appraisal 259 appraised abiraterone following prior treatment with chemotherapy. The brand name has been added to the scope background section.

Section	Consultees	Comments	Action
	Royal College of Physicians on behalf of NCRI Clinical Studies Group/Royal College of Physicians/Royal College of Radiologists/Joint Collegiate Council on Oncology/Association of Cancer Physicians	yes	Comment noted.
Population	British Uro-oncology Group (BUG)	Yes	Comment noted.
	CSAS	This is appropriately defined. Separate consideration could be given to symptomatic and asymptomatic men, or according to Karnofsky Performance Status score, particularly given current restrictions placed on the use of docetaxel.	Comment noted. The population has been amended to specify the population as asymptomatic or mildly symptomatic to correspond with the licence indication. Following the scoping workshop, consultees concluded that in the absence of the results from the trial they had no clinical or biological evidence to support subgroups based on performance scores.

Section	Consultees	Comments	Action
	Janssen	Janssen would like the population in the scope to reflect our anticipated licence and to include “asymptomatic and mildly symptomatic” as outlined below: “Men with asymptomatic or mildly symptomatic metastatic, castration-resistant prostate cancer who have not received prior cytotoxic chemotherapy or biologic therapy.”	Comment noted. Following the scoping workshop, consultees agreed change the population to patients who were either asymptomatic or mildly symptomatic in line with the expected licence indications.
	NHS Bradford and Airedale	This is appropriately defined. Separate consideration could be given to symptomatic and asymptomatic men, or according to Karnofsky Performance Status score, particularly given current restrictions placed on the use of docetaxel.	Comment noted. The population has been amended to specify the population as asymptomatic or mildly symptomatic to correspond with the expected licence indications. Following the scoping workshop, consultees concluded that in the absence of the results from the trial they had no clinical or biological evidence to support subgroups based on performance scores.
	The Prostate Cancer Charity	Biologic therapy should be defined to provide context to the definition of the population.	Following the scoping workshop, reference to biologic therapy has been removed. Consultees noted that treatment with biologic therapy does not represent the current practice in the NHS.
	Royal College of Physicians on	We would suggest splitting the assessment into 2 groups 1. asymptomatic / mildly symptomatic	Comments noted. The population has been amended

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	behalf of NCRI Clinical Studies Group/Royal College of Physicians/Royal College of Radiologists/Joint Collegiate Council on Oncology/Association of Cancer Physicians	2. symptomatic castration resistant is the best term	to specify the population as asymptomatic or mildly symptomatic to correspond with the expected licence indication.
	Sanofi UK	We believe the population is defined accurately, however please see comment below on comparators and the relevance of these to the patient population included in the abiraterone trial.	Comment noted.
Comparators	British Uro-oncology Group (BUG)	Cabazitaxel should be mentioned here. Important to note that treatment is highly individualised	Comment noted. During the scoping workshop, consultees discussed whether any other chemotherapy options were routinely used, but agreed that docetaxel was the only appropriate comparator for most patients with metastatic castration-resistant prostate cancer at this time.
	CSAS	Docetaxel is licensed for use in combination with prednisone or prednisolone, as a treatment option for men with hormone-refractory metastatic prostate cancer with Karnofsky performance-status score of 60% or more. This is the most appropriate comparator for chemotherapy-naive castration-resistant prostate cancer. Mitoxantrone is not licensed for use in prostate cancer. NICE TA101 (June 2006) highlighted that "Mitoxantrone is widely used in the UK for hormone-	Comments noted. During the scoping workshop, consultees agreed that that docetaxel was the only appropriate chemotherapy comparator for most patients with metastatic castrate-resistant prostate

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		refractory metastatic prostate cancer patients who are fit for chemotherapy…a combination of mitoxantrone and prednisolone has come to be accepted as the standard care for this group of patients". The current level of unlicensed mitoxantrone use as an alternative to docetaxel should be assessed. A corticosteroid is listed in NICE CG58 as a third-line hormonal treatment option for castration-resistant prostate cancer. Dexamethasone (0.5 mg daily) is most commonly used. Either dexamethasone or prednisolone monotherapy could be considered alternative comparators to abiraterone and prednisolone combination. Supportive care options are appropriate, though mitoxantrone in combination with prednisolone may be considered as above as an alternative treatment, rather than a palliative option.	cancer. Clinical experts stated that mitoxantrone was not in wide use in the NHS for this patient group. It was therefore agreed that mitoxantrone should be removed as a comparator. Clinical experts expressed the view that corticosteroids formed part of best supportive care and would generally not be used outside best supportive care regimens.
	Janssen	Janssen suggests that Docetaxel may not be an appropriate comparator for abiraterone in this patient population as docetaxel is used only in patients symptomatic metastatic disease and not in asymptomatic or mildly symptomatic disease. The best supportive care comparator is an appropriate comparator as patients with asymptomatic or mildly symptomatic metastatic disease in the UK will often be on best supportive care whilst being actively monitored for disease progression to symptomatic disease when patients may be considered for chemotherapy. Janssen believes that mitoxantrone and biphosphonates would not be used in this asymptomatic or mildly symptomatic patient population and therefore should not be included within best supportive care comparator. Also to alleviate confusion on steroid use Janssen suggests rewording the definition of best supportive care to the following: “Best supportive care (this may include chronic steroid use, radiotherapy, radiopharmaceuticals, analgesics, and further hormonal therapies)”	Comments noted. Docetaxel remains in the list of comparators because the recommendations in TA101 include patients who are asymptomatic or mildly symptomatic, and clinicians have stated at the scoping workshop that docetaxel is increasingly used for this patient group, and because of the lack of clear clinical criteria to identify the patient group in the CHMP indication.
	NHS Bradford and Airedale	Docetaxel is licensed for use in combination with prednisone or prednisolone, as a treatment option for men with hormone-refractory metastatic prostate	Comments noted. During the scoping workshop, consultees

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		cancer with Karnofsky performance-status score of 60% or more. This is the most appropriate comparator for chemotherapy-naive castration-resistant prostate cancer. Mitoxantrone is not licensed for use in prostate cancer. NICE TA101 (June 2006) highlighted that "Mitoxantrone is widely used in the UK for hormone-refractory metastatic prostate cancer patients who are fit for chemotherapy…a combination of mitoxantrone and prednisolone has come to be accepted as the standard care for this group of patients". The current level of unlicensed mitoxantrone use as an alternative to docetaxel should be assessed. A corticosteroid is listed in NICE CG58 as a third-line hormonal treatment option for castration-resistant prostate cancer. Dexamethasone (0.5 mg daily) is most commonly used. Either dexamethasone or prednisolone monotherapy could be considered alternative comparators to abiraterone and prednisolone combination. Supportive care options are appropriate, though mitoxantrone in combination with prednisolone may be considered as above as an alternative treatment, rather than a palliative option.	agreed that that docetaxel was the only appropriate chemotherapy comparator for most patients with metastatic castration-resistant prostate cancer at this time. Clinical experts stated that mitoxantrone was not in wide use in the NHS for this patient group. It was therefore agreed that mitoxantrone should be removed as a comparator. Clinical experts expressed the view that corticosteroids formed part of best supportive care and would generally not be used outside best supportive care treatments.
	The Prostate Cancer Charity	We do not have enough evidence to comment on this aspect without the published phase III trial data for this indication.	Comment noted.
	Royal College of Physicians on behalf of NCRI Clinical Studies Group/Royal College of Physicians/Royal College of Radiologists/Joint Collegiate Council on Oncology/Assoc	At present men would be offered Docetaxel if fit enough for it. If not fit enough then best supportive care defined as analgesia, palliaitve radiotherapy, low dose dexamethasone 0.5mg od and strontium. Zoledronic acid can currently only be given in exceptional circumstances in Scotland	Comment noted. During the scoping workshop, consultees agreed that best supportive care should include radiotherapy, radiopharmaceuticals, analgesics, bisphosphonates, further hormonal therapies, and corticosteroids.

Section	Consultees	Comments	Action
	iation of Cancer Physicians		

Section	Consultees	Comments	Action
	Sanofi UK	Docetaxel is the standard of care for the first-line treatment of metastatic castration-resistant prostate cancer (CRPC). It is the only agent approved by NICE for this indication and until abiraterone was the only agent to have demonstrated a survival benefit in first-line CRPC. As such, we believe docetaxel is the most appropriate comparator for abiraterone. We note that the abiraterone trial was conducted in patients with castration-resistant disease and good performance status (ECOG 0 - 1). These patients would currently be considered for docetaxel chemotherapy. Current best practice is to initiate docetaxel as soon as the disease is demonstrably castration-resistant and shows signs of progression, to ensure patients receive maximum benefit while they are fit enough to tolerate chemotherapy. We do not consider best supportive care to be an appropriate comparator. In the context of first-line treatment of metastatic CRPC, best supportive care is typically only used for patients who have poorer performance status and are hence ineligible for docetaxel chemotherapy, or who have refused chemotherapy, or for whom chemotherapy is contraindicated. This is a different patient population to that in the abiraterone trial, which included only patients with good performance status (ECOG 0 -1) who would currently all be considered for docetaxel chemotherapy. Further, we do not believe mitoxantrone should be included within "best supportive care". Mitoxantrone is an active chemotherapy agent. It has demonstrated a significant impact on symptom control (although not survival) in the first-line setting. In addition, although comparatively well-tolerated for a chemotherapy, mitoxantrone is still associated with adverse events and tolerability issues. Therefore mitoxantrone is unsuitable for the poorer performance status patients who would be considered for best supportive care following progression after hormone therapy. Patients whose disease has become castration-resistant and who are eligible for chemotherapy would normally receive first-line docetaxel, with mitoxantrone often used as a second-line agent, whereas patients who are not eligible for chemotherapy would not be considered for either docetaxel or mitoxantrone chemotherapy.	Comments noted. During the scoping workshop, consultees agreed that that docetaxel was the only appropriate chemotherapy comparator for most patients with metastatic castration-resistant prostate cancer at this time. The clinical experts at the scoping workshop stated that best supportive care should be considered a comparator option for patients with metastatic castration-resistant prostate cancer not previously treated with chemotherapy, because not all patients receive chemotherapy. The Appraisal Committee will consider the evidence available and assess its relevance in relation to the indicated population. Consultees felt that mitoxantrone was not in wide use in the NHS for this patient group. It was therefore agreed that mitoxantrone should be removed from the comparator list.

Section	Consultees	Comments	Action
Outcomes	British Uro-oncology Group (BUG)	As long as pain improvement and prolongation of developing new pain is captured	Comment noted. During the scoping workshop, consultees expressed the view that the effect of pain would be captured in the health-related quality of life outcome.
	CSAS	Effect on symptoms could be considered as an additional outcome, particularly relating to pain.	Comment noted. During the scoping workshop, consultees expressed the view that the effect of pain would be captured in the health-related quality of life outcome.
	Janssen	In addition to the outcomes in the draft scope, Janssen suggests that radiographic progression free survival be included as an outcome of interest. Abiraterone provides patients with a treatment option where currently there are limited options; therefore radiographic confirmation of progression may enable clinicians to identify patients who should stop treatment with abiraterone so that other treatment options such as chemotherapies or biologic therapies can be considered. Therefore in this patient population, radiographic progression free survival is most likely to be an appropriate progression-related outcome. Other outcomes to be considered should also include: Time to PSA progression based on PCWG2 criteria, Time to deterioration of ECOG score, Time to initiation of cytotoxic therapies, Time to opiate use.	Following the scoping workshop, consultees noted that many of the suggested outcomes were already covered in the list of current outcomes, in particular by the progression-free survival outcome. Radiographic progression-free survival has been added.
	NHS Bradford and Airedale	Effect on symptoms could be considered as an additional outcome, particularly relating to pain	Comment noted. During the scoping workshop, consultees expressed the view that the effect of pain would be captured in the health-related quality of life outcome.

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	The Prostate Cancer Charity	We agree with the clinical outcomes identified 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. 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. For example, as abiraterone is an oral agent, its administration is likely to be comparatively more straightforward than, for example, chemotherapy, and can offer a man with advanced disease greater flexibility to lead a more 'normal' life for the period of benefit.	Comments noted. The Appraisal Committee will consider all outcomes supported by the evidence available. Moreover, section 5.4.1 of the 'Guide to the methods of technology appraisal' (NICE, 2008) states that the measurement of changes in HRQL should be reported directly from patients.
	Royal College of Physicians on behalf of NCRI Clinical Studies Group/Royal College of Physicians/Royal College of Radiologists/Joint Collegiate Council on Oncology/Association of Cancer Physicians	Yes, We think these are reasonable	Comment noted.
	Sanofi UK	We believe these are appropriate.	Comment noted.

Section	Consultees	Comments	Action
Economic analysis	British Uro-oncology Group (BUG)	Appropriate	Comment noted.
	The Prostate Cancer Charity	We do not have evidence to enable us to comment on this area	Comment noted.
	Royal College of Physicians on behalf of NCRI Clinical Studies Group/Royal College of Physicians/Royal College of Radiologists/Joint Collegiate Council on Oncology/Association of Cancer Physicians	For patients who are fit for chemotherapy then would want to use sequential treatment. If not fit for chemotherapy then abiraterone alone	Comment noted.
	Sanofi UK	We agree with the approach put forward in the scope; we consider the appropriate time horizon is the lifetime of the patient.	Comment noted.
Equality	British Uro-oncology Group (BUG)	There should not be any issues regarding equality as patients will all be under the care of specialist oncologists.	Comment noted.
	CSAS	There are no specific issues relating to the technology, but in the UK, black Caribbean and black African men have approximately two to three times the risk of being diagnosed or dying from prostate cancer than white men. Asian men generally have a lower risk than the national average.	Comment noted. Differences in prevalence alone cannot be addressed within a technology appraisal.

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	NHS Bradford and Airedale	There are no specific issues relating to the technology, but in the UK, black Caribbean and black African men have approximately two to three times the risk of being diagnosed or dying from prostate cancer than white men. Asian men generally have a lower risk than the national average.	Comment noted. Differences in prevalence alone cannot be addressed within a technology appraisal.
	The Prostate Cancer Charity	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	Comment noted. Differences in prevalence alone cannot be addressed within a technology appraisal. The Committee will assess whether their recommendation restricts access to the technology for any group of people. During consultation on the scope, no evidence was received of differential access to therapy or prognosis in this group. No changes to the scope are required.

Section	Consultees	Comments	Action
	Royal College of Physicians on behalf of NCRI Clinical Studies Group/Royal College of Physicians/Royal College of Radiologists/Joint Collegiate Council on Oncology/Association of Cancer Physicians	No concerns	Comment noted.
Other considerations	British Uro-oncology Group (BUG)	Comparison with cabazitaxel. Time since taxane treatment should not be a consideration as this was not addressed in the pivotal trial.	Comments noted. During the scoping workshop, consultees discussed whether any other chemotherapy options were routinely used, but agreed that that docetaxel was the only appropriate comparator for most patients with metastatic castration-resistant prostate cancer at this time. Time since taxanes is not relevant to this scope as the scope population is defined metastatic castration-resistant prostate cancer not previously treated with chemotherapy.
Innovation	British Uro-oncology Group	Yes, this is a significant additional therapy that has the potential to prolong survival for a large number of men.	Comment noted. The Committee will consider the

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	(BUG)	It has changed our understanding of the pathogenesis of this disease and its' treatment. It truly is a 'step-change' in the management of this disease. As a tablet it can be dispensed immediately and will have relatively little impact on clinics. Abiraterone offers significant clinical benefits, including pain relief and delay of pain recurrence while preventing skeletal related events (ASCO 2011). Results from PIVOTAL phase III trial COU-AA-301, pre-planned interim results presented in 2010, with full paper submitted to NEJM 2011. Latest overall survival in the phase 3 trial was 15.8 months in the abiraterone group and 11.2 months in the placebo group (P < .0001); (American Society of Clinical Oncology Meeting 2011). Abiraterone offers significant clinical benefits, including pain relief and delay of pain recurrence while preventing skeletal related events (ASCO 2011).	innovative nature of abiraterone, specifically if the innovation adds demonstrable and distinctive benefits of a substantial nature which may not have been adequately captured in the QALY measure. No changes to the draft scope required.
	CSAS	No additional comments.	Comment noted.
	Janssen	Abiraterone is an oral medication with a unique mechanism of action, blocking testosterone production at three sites of androgen synthesis, which has previously been demonstrated to deliver an overall survival benefit in patients with metastatic disease whose disease has progressed on or after docetaxel based therapy. Adverse events experienced by patients in this trial were predominantly grade 1 and 2. Abiraterone will provide an oral treatment option that can be taken in the patient's home. This equates to a step-change for patients with asymptomatic and mildly symptomatic metastatic disease, providing an active treatment where currently there are no treatment options other than waiting for disease progression when chemotherapy may be considered. Abiraterone is an oral treatment that is well tolerated and as such, is likely to offer patient benefits such as not having to travel to hospital for treatment and not having to have undergo i/v infusions which are unlikely to be accounted for	Comment noted. The Committee will consider the innovative nature of abiraterone, specifically if the innovation adds demonstrable and distinctive benefits of a substantial nature which may not have been adequately captured in the QALY measure. No changes to the draft scope required.

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		in the in the QALY calculation. Assessment of these benefits may be taken via patient interviews and/or a patient preference study.	
	The Prostate Cancer Charity	Yes, the technology could potentially change the management of castration-resistant prostate cancer but we are not able to comment further without seeing the relevant phase III trial data.	Comment noted.
	Royal College of Physicians on behalf of NCRI Clinical Studies Group/Royal College of Physicians/Royal College of Radiologists/Joint Collegiate Council on Oncology/Association of Cancer Physicians	This would be a significant advance for men who are not fit enough to ever receive chemotherapy as it may well prolong survival and maintian quality of life. For men who would otherwise receive chemotherapy it is unclear as to the best scheduling of treatment. Should it be chemotherapy first and abiraterone second or vise a versa. Currently we do not have an answer however not to have the option of abiraterone in this patient group would be a concern. This drug could reduce costs associated with palliaitve/ best supportive care This is a step change. It is also important to recognise that the reason for the change in terminology ('hormone resistant' to castrate-resistant') is because of the understanding resulting from the abiraterone studies. That is, that a substantial number of castrate-resistant tumours remain driven by androgen receptor mediated signalling, and that prostate cancer cells themselves are able to synthesise and respond to low levels of androgen. This is the primary reason why abiraterone (and in the future other drugs of its class), by inhibiting such synthesis, produces clinical responses. *Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?* Some of the responding men might have extremely long survival times, far in excess of anything previously recorded in CRPC. Such men might delay or even avoid treatment with docetaxel.	Comment noted. The Committee will consider the innovative nature of abiraterone, specifically if the innovation adds demonstrable and distinctive benefits of a substantial nature which may not have been adequately captured in the QALY measure. No changes to the draft scope required.
Questions for	The Prostate	It would be helpful to relate this appraisal to the technology appraisal in	Comment noted. NICE

Section	Consultees	Comments	Action
consultation	Cancer Charity	preparation on abiraterone (in comination with prednisolone) for the treatment of metastatic castrate resistant prostate cancer following previous cytotoxic chemotheraphy. Conducting the appraisals together would help avoid duplication of effort and confusion over the similar appraisals.	guidance on abiraterone for the treatment of castration-resistant metastatic prostate cancer previously treated with a docetaxel-containing regimen was published in June 2012 (NICE technology appraisal 259), and there is no evidence to suggest that this guidance needs to be reviewed. The current appraisal is for a different patient group and the only timely way to develop recommendations is through the Single Technology Appraisal process. Consultees agreed with that at the scoping workshop.
	Royal College of Physicians on behalf of NCRI Clinical Studies Group/Royal College of Physicians/Royal College of Radiologists/Joint Collegiate Council on Oncology/Association of Cancer Physicians	*Has the population been appropriately defined? For example, is the term 'castrate-resistant' more appropriate than 'castration-resistant'?* Either term is satisfactory *Have the most appropriate comparators for abiraterone for the treatment of chemotherapy naïve, metastatic, castration-resistant prostate cancer been included in the scope? In particular* • *Should any other chemotherapy treatments be included?* No • *How should 'best supportive care' be defined?* Increasingly hard to define, since these patients might be considered for treatment with radiotherapy, radiopharmaceuticals, analgesics,	Comments noted. See comments above regarding the best supportive care comparator.

Section	Consultees	Comments	Action
		bisphosphonates, other hormonal therapy (eg stilboestrol) and mitoxantrone, with or without corticosteroids, as well as steroids alone. Best left undefined. We would seek clarification about use of corticosteroids, such as dexamethasone, as a comparator. The pre-chemo space includes men progressing after CAB, and also men progressing after CAB and dexamethasone. Some believe that cost-effective use of abiraterone in the UK might well be to restrict it to the post-dexamethasone setting. The other comparator that may or may not need to be stated explicitly, is the use of abiraterone in the post-docetaxel setting. It is possible that using abiraterone later in the disease might be as effective, and might also be cheaper because patients will stay on drug for less time *Are docetaxel and best supportive care used in the same circumstances? Or are they used for particular patient groups? If so what are the characteristics of these patients groups?* Docetaxel might, overall, be used in a younger, fitter group of men than might be the case for abiraterone, which could be given to men not fit enough for docetaxel. BSC is also more likely in men refusing chemotherapy. *Are there subgroups of men in whom abiraterone is expected to be more clinically effective and cost effective or other groups that should be examined separately? For instance, is abiraterone likely to be more effective in asymptomatic or mildly symptomatic men?* No, not that is known	The scope of this appraisal is metastatic castration-resistant prostate cancer not previously treated with chemotherapy. A separate appraisal is published for metastatic, castration-resistant prostate cancer following previous cytotoxic chemotherapy (NICE technology appraisal 259). Comment noted.

Section	Consultees	Comments	Action
Additional comments on the draft scope	The Prostate Cancer Charity	There is a mistake in the second sentence of the second paragraph in the section 'The technology' on page 2. It should read: "It is being studied in clinical trials..."	Comment noted. Background section has been changed accordingly.
	Royal College of Physicians on behalf of NCRI Clinical Studies Group/Royal College of Physicians/Royal College of Radiologists/Joint Collegiate Council on Oncology/Association of Cancer Physicians	*NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process* Appropriate.	Comment noted.

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

Healthcare Improvement Scotland
Marie Curie Cancer Care
Prostate Action
Royal College of Pathologists
Department of Health
Medicines and Healthcare products Regulatory Agency

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

Abiraterone acetate for the treatment of metastatic castration-resistant prostate cancer not previously treated with chemotherapy

Response to consultee and commentator comments on the provisional matrix of consultees and commentators (pre-referral)

Version of matrix of consultees and commentators reviewed: Provisional matrix of consultees and commentators sent for consultation					
Summary of comments, action taken, and justification of action:					
1.	*Proposal:*	*Proposal made by:*		*Action taken:* Removed/Added/Not included/Noted	*Justification:*
2.	Add: West Wales Prostate Cancer Support Group	Janssen		Not included	This is a local group, it therefore does not meet the inclusion criteria.

3.	Add: Prostate Brachytherapy Advisory Group	Janssen		Not included	This population of interest in this appraisal is adults with metastatic castration-resistant prostate cancer. Brachytherapy is a treatment option for patients with localised disease only
4.	Add: Ulster Cancer Foundation	Janssen		Not included	This is a local group, it therefore does not meet the inclusion criteria.
5.	Add: Glaze	Janssen		Added	This group meets the inclusion criteria and has been added to the matrix.
6.	Add: Prostate Cancer Support Association	Janssen		No action	Organisation has been dissolved, website refers to Prostate Cancer Support Federation, who are on the matrix.
7.	Add: Prostate UK	Janssen		No action	We presume you are referring to Prostate Cancer UK, who are on the matrix.

8.	Add: Prostaid	Janssen		Not included	Website states that “We serve the local cancer care network in Leicestershire, Rutland & Northamptonshire”. Therefore this is a local group, it therefore does not meet the inclusion criteria.
9.	Add: BOPA (British Oncology Pharmacy Association)	Janssen		Not included	Organisation has requested that they are not included in NICE Technology Appraisals as interests covered by Cancer Networks Pharmacist Forum