National Institute for Health and Care Excellence

Health Technology Evaluation

Olaparib with abiraterone for untreated hormone-relapsed metastatic prostate cancer [ID3920]
Response to stakeholder organisation comments on the draft remit and draft scope

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Prostate Cancer UK	Prostate cancer UK welcomes the evaluation of olaparib used in conjunction with abiraterone for untreated, metastatic hormone resistant prostate cancer. There are several treatments available in the metastatic castrate resistant setting, such as docetaxel, abiraterone, enzalutamide, or cabazitaxel. Radium 223 is a further last line treatment. There are currently no precision treatments available for prostate cancer. However, there still remains a strong need for further treatments in this indication that offer good clinical benefit and improvement in progression free survival and it is clear from the evidence in the PROpel trial that this drug combination could fit this remit. Should the proposed appraisal recommend that abiraterone with olaparib is effective for the above indication, it will help to provide and improve standardised access and increased treatment choice to a group of patients who currently have a restricted range of treatments available. We also believe that the single technology appraisal route is appropriate in this instance.	Thank you for your comment. No action required.

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	AstraZeneca	We agree with the appropriateness of evaluating this topic, and the proposed evaluation route of a 'single technology appraisal'.	Thank you for your comment. No action required.
Wording	Prostate Cancer UK	We believe the wording reflects the clinical effectiveness issues.	Comment noted. No action required.
	AstraZeneca	The proposed wording of the remit is currently reflective of the clinical and cost-effectiveness issues. However, we would like to note that: • The full wording of the remit aligned with the clinical study population is "patients with metastatic castration-resistant prostate cancer (mCRPC) who have received no prior cytotoxic chemotherapy or new hormonal agents (NHAs) at metastatic castration-resistant prostate cancer (mCRPC) stage (NCT03732820)". • [redacted]	Comment noted. The term "at hormone-relapsed metastatic stage" has been added to the scope to clarify the intended objective. Following EMA approval, the population has been updated to hormone-relapsed metastatic prostate cancer in people for whom chemotherapy is not clinically indicated.
Timing Issues	Prostate Cancer UK	The timing of this appraisal appears appropriate. However, it should be noted that as with any evaluation of a cancer drug which shows strong evidence of progression free survival in comparison to the comparators and/or standard of care, we would suggest that there is an urgency considering the initial results of the PROpel trial (24.8 vs. 16.6 months by investigator assessment and 27.6 vs. 16.4 months by blinded independent central review in the abiraterone and olaparib and abiraterone and placebo arms, respectively).	Thank you for your comment. NICE will schedule this topic into its work programme, depending on the company's intended submission date.

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		Patients who are considered to be in this indication, especially those who are contra-indicated to docetaxel and thus would not be eligible to have it as an alternative treatment option, would greatly benefit from olaparib with abiraterone and its subsequent increase in progression free survival in comparison to abiraterone alone. We also would suggest that those patients with more aggressive prostate cancers would benefit from a more urgent approach to this evaluation, as this would allow this drug combination to be available faster to those who may be facing a shorter timeframe to progression and possible death from their prostate cancer. It is imperative for these patients to receive the best standard of care in a timely fashion which would allow for the longest potential time to progression.	
	AstraZeneca	No comment.	Thank you for your comment. No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Prostate Cancer UK	We consider the background information to be sufficient.	Comment noted. No action required.
	AstraZeneca	We agree with the accuracy of the background information.	Comment noted. No action required.
Population	Prostate Cancer UK	In clinical practice we expect patients to have previously been treated with docetaxel or a NHA whilst metastatic hormone sensitive. We would need	Thank you for your comment. The

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		more clarity on patients previously treated with enzalutamide and whether they would be eligible for this combined treatment of abiraterone and olaparib as patients in the trial were allowed a previous NHA as long as treatment had ceased more than or equal to 12 months prior to enrolment. Current policy only allows for treatment with one novel hormonal agent but it isn't clear if this also applies to combination therapies such as this. Because of the Covid-19 pandemic many patients will have been receiving enzalutamide and so may not be eligible.	appropriate population will be decided according to the company's marketing authorisation, current commercial arrangements, and NHS practice.
	AstraZeneca	The PROpel (NCT03732820) clinical study population is "patients with metastatic castration-resistant prostate cancer (mCRPC) who have received no prior cytotoxic chemotherapy or new hormonal agents (NHAs) at metastatic castration-resistant prostate cancer (mCRPC) stage". [redacted]	Comment noted. The term "at hormone-relapsed metastatic stage" has been added to the scope to clarify the intended objective. Following EMA approval, the population has been updated to people with hormone-relapsed metastatic prostate cancer for whom chemotherapy is not clinically indicated.
Subgroups	Prostate Cancer UK	Prostate Cancer UK acknowledges that the subgroups with HRR status (BRCA1/2 and ATM genes) will be considered in the appraisal if the evidence from the trial allows. The PROfound trial demonstrated significant imaging-based progression-free survival and overall survival benefits with olaparib alone in patients with metastatic castrate resistant prostate cancer	Thank you for your comment. No action required.

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		harbouring BRCA1, BRCA2, and ATM mutations whose disease had progressed on a novel hormonal agent. With that in mind we consider this group to potentially receive considerable clinical effectiveness from treatment from abiraterone with olaparib, and could show increased benefit from treatment with this combination than those patients without any mutation.	
	AstraZeneca	Although, patients with homologous recombination repair mutations (HRRm) were included in the study as a pre-specified subgroup, the PROpel Phase III clinical study was designed to examine the combined anti-tumour effect through interactions between poly(adenosine diphosphate–ribose) polymerase (PARP) inhibitors and the androgen receptor signalling pathway, and as such was conducted in a biomarker-unselected population.	Comment noted. The subgroups are intended to be considered only if the evidence allows. No action required.
Comparators	Prostate Cancer UK	We consider the comparators to be sufficient but we feel it should be noted that docetaxel is not always tolerated by patients who are older or who may have comorbidities and so would not be a suitable comparator for this group of patients.	Thank you for your comment. Following EMA approval, the population has been updated to people with hormone-relapsed metastatic prostate cancer for whom chemotherapy is not clinically indicated. Docetaxel has been removed as a comparator.
	AstraZeneca	The proposed label and draft remit considers olaparib with abiraterone in first-line metastatic hormone-relapsed prostate cancer in patients who have not received NHAs. Hence, it is anticipated that an overwhelming majority of	Thank you for your comment. Following EMA approval, the

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		eligible patients would be offered an NHA in the first line hormone-relapsed metastatic setting, with docetaxel used later in the treatment pathway. Olaparib with abiraterone in the first line metastatic hormone-relapsed setting is expected to displace abiraterone [per TA387] and enzalutamide [TA377]; therefore, the we consider these as the relevant comparators for this appraisal.	population has been updated to people with hormone-relapsed metastatic prostate cancer in people for whom chemotherapy is not recommended. Docetaxel has been removed as a comparator.
Outcomes	Prostate Cancer UK	We consider the outcomes to be sufficient.	Comment noted. No action required.
	AstraZeneca	Time-to-second progression (PFS2) is an important patient outcome and should be included.	Thank you for your comment. The outcomes have been standardised in line with recent appraisals for the indication. No action required.
	Janssen	Please could the outcome of 'progression free survival' be disambiguated to read 'radiographic progression free survival'. We also note response rate is unlikely to be a relevant outcome.	Thank you for your comment. The outcomes have been standardised in line with recent appraisals for the indication. No action required.

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Equality	Prostate Cancer UK	We consider the draft remit to be sufficient with regards to the equality aims.	Comment noted. No action required.
	AstraZeneca	No issues identified.	Thank you for your comment.
Other considerations	AstraZeneca	No comment.	Comment noted.
Questions for consultation	AstraZeneca	**Where do you consider olaparib with abiraterone, will fit into the existing care pathway for hormone-relapsed metastatic prostate cancer?** • Per the proposed label, it is anticipated that this indication will fit into the biomarker unselected patients in first line metastatic hormone-relapsed prostate cancer displacing abiraterone and enzalutamide. **Have all the relevant comparators for olaparib with abiraterone been included in the scope?** • As outlined in the comments on the comparators, abiraterone and enzalutamide are the relevant comparators. **Is it appropriate to exclude treatments recommended after chemotherapy as comparators?** • Yes, this is consistent with the PROpel (NCT03732820) clinical study design which focuses on patients with metastatic castration-resistant prostate cancer (mCRPC) who have received no prior cytotoxic chemotherapy or new hormonal agents (NHAs) at the metastatic castration-resistant prostate cancer (mCRPC) stage.	Thank you for your comment. All potentially relevant comparators have been identified, in line with NICE's method guide. No action required. The appropriate population will be decided according to the company's marketing authorisation, current commercial arrangements, and NHS practice. No action required. The outcomes have been standardised in line with recent

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		Are interim treatment option recommendations by NHS England for prostate cancer during the COVD-19 pandemic likely to influence the treatment pathway? • Our understanding is that any relevant COVID-19 interim guidance has been superseded by current NICE recommendations. **Have all the appropriate outcomes been captured?** • As discussed above, time-to-second progression (PFS2) is an important patient outcome and should be included. **Do you consider radiological progression free survival (rPFS) to be an appropriate outcome measure for hormone-relapsed metastatic prostate cancer?** • rPFS is an important endpoint used in multiple contemporary prostate cancer clinical studies and is a particularly relevant outcome for metastatic hormone-relapsed prostate cancer patients. **Are there any subgroups for which olaparib with abiraterone would be expected to be more clinically effective and cost-effective?** • The PROpel clinical study was designed to examine the combined anti-tumour effect through interactions between poly(adenosine diphosphate–ribose) polymerase (PARP) inhibitors and the androgen receptor signalling pathway, and as such was conducted in a biomarker-unselected population. However, patients with homologous recombination repair mutations (HRRm) were included as a pre-specified subgroup. **Would it be appropriate to consider olaparib with abiraterone as first-line treatment irrespective of HRR status?**	appraisals for the indication. No action required.

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		• Yes, the pivotal clinical study, PROpel, was designed to address the unmet need in a biomarker-unselected population. **Would olaparib with abiraterone be a candidate for managed access?** • Potentially, although details to be confirmed **Do you consider olaparib with abiraterone to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?** • The proposed mechanism of action involving combined PARP inhibition and androgen receptor signalling means that the efficacy of a gene-targeted therapy in prostate cancer can be assessed in a biomarker-unselected population for the first time. • As recently published, when compared to abiraterone, olaparib in combination with abiraterone results in was significantly longer and clinically meaningful median PFS (24.8 vs. 16.6 months; hazard ratio, 0.66; 95% confidence interval [CI], 0.54 to 0.81; P<0.001). Despite immature overall survival data, (28.6% maturity), a relative reduction in risk of death by 14% is observed (hazard ratio, 0.86; 95% CI, 0.66 to 1.12; P=0.29). • Finally, in June 2022, olaparib in this indication received Innovation Passport designation (olaparib in combination with abiraterone and prednisone or prednisolone in the treatment of adult patients with metastatic castration resistant prostate cancer).	

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

N/A.