National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Padeliporfin for treating localised prostate cancer

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

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

Section	Consultee/ Commentator	Comments [sic]	Action
Appropriateness	*Would it be appropriate to refer this topic to NICE for appraisal?*		
	British Association of Urological Surgeons (BAUS) Section of Oncology	We would suggest awaiting the results of the phase III study or that you seek to get sight of the data.	Comment noted. No changes to the scope are needed.
	Prostate Cancer UK	Yes. Prostate cancer is the most common cancer in men. In England, more than 38,000 men are diagnosed with prostate cancer every year and more than 9,000 men will die from it each year. Prostate cancer treatment should therefore be considered a priority issue for NICE.	Comment noted. The scope has been updated to include the most recent epidemiological data available.

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	STEBA Biotech	Yes	Comment noted. No changes to the scope are needed.
Wording	*Does the wording of the remit reflect the issue(s) of clinical and cost effectiveness about this technology or technologies that NICE should consider?*		
	BAUS Section of Oncology	Yes	Comment noted. No changes to the scope are needed.
	Prostate Cancer UK	Yes	Comment noted. No changes to the scope are needed.
	STEBA Biotech	Yes	Comment noted. No changes to the scope are needed.
Timing Issues	BAUS Section of Oncology	Phase III results should be in the public domaine Q2 2016	Comment noted. Normally, NICE aims to provide draft guidance to the NHS within 6 months of the date when the marketing authorisation for a technology is granted. However, at the request of the company the start of this appraisal has been delayed.

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	Prostate Cancer UK	It would be of benefit to men with localised prostate cancer to appraise this technology as soon as possible because the active comparators are radical treatment options that cause life-changing and life-limiting side-effects.	Comment noted. Normally, NICE aims to provide draft guidance to the NHS within 6 months of the date when the marketing authorisation for a technology is granted. However, at the request of the company, the start of this appraisal has been delayed.
	STEBA Biotech	No particular urgency	Comment noted. Normally, NICE aims to provide draft guidance to the NHS within 6 months of the date when the marketing authorisation for a technology is granted. However, at the request of the company the start of this appraisal has been delayed.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	BAUS Section of Oncology	Fine but it does not take account of modern methods of risk stratification.	Comment noted. This section of the scope aims to provide a brief overview of the background for the appraisal and includes a description of the risk stratification described in NICE clinical guideline 175; additional details may be considered by the committee, if appropriate, at the time of the appraisal.
	Prostate Cancer UK	In paragraph two, we recommend replacing the second sentence with: "Localised prostate cancer doesn't usually cause any symptoms. However, symptoms can include: difficulty in passing urine, passing urine more frequently than usual (especially at night), pain when passing urine and blood in the urine." In paragraph three, we recommend replacing the first sentence with: "The incidence of prostate cancer increases with age and is higher in Black African and African-Caribbean men and men with a family history of the disease." In paragraph three, we recommend replacing the second sentence with: "On average, more than 38,000 men are diagnosed with prostate cancer every year in England." (Reference: Office for National Statistics. Cancer Statistics Registrations, England (1995-2013). 2015. Available from:	The background section of the scope has been updated.

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		http://www.ons.gov.uk/ons/publications/re-reference-tables.html?edition=tcm%3A77-394268).	
	STEBA Biotech	The background provides a good overview. For low risk prostate cancer patients, it could be mentioned that radical prostatectomy and radiotherapy are acceptable options for patients who chose it	The background section of the scope has been updated.
The technology/ intervention	BAUS Section of Oncology	Yes, but more could be made of the fact that this technology offers a different way to treat prostate cancer that diverges from the standard of care which is directed at the whole gland. This technology is will be directed to the cancer or to part of the gland.	Comment noted. This section of the scope aims to provide a brief summary of the technology; additional details may be considered by the committee, if appropriate, at the time of the appraisal.
	Prostate Cancer UK	*Is the description of the technology or technologies accurate?* Yes	Comment noted. No changes to the scope are needed.
	STEBA Biotech	It could be mentioned that the photo-activation is only local and that the mechanism of action is based on vascular occlusion.	Comment noted. The technology section states that padeliporfin is used with vascular-targeted photodynamic therapy and has been updated to state that this is delivered by interstitial optical fibres from a laser device.

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Population	BAUS Section of Oncology	The classification of risk is no longer straight forward as modern methods of risk stratification identify new and different populations - we do not as yet know what their risk is.	Comment noted. The marketing authorisation for padeliporfin has now been granted and stipulates the risk eligibility criteria. Padeliporfin will be appraised within the population covered by its marketing authorisation.
	Prostate Cancer UK	The population is defined appropriately.	Comment noted. The population has been updated to reflect the population covered by by the marketing authorisation which has now been granted.
	STEBA Biotech	Among low risk prostate cancer patients, only those with either 1 positive core of 3 to 5mm or those with 2-3 positive cores of less than 5mm should be included (inclusion population of the European Phase III study)	Comment noted. The marketing authorisation for padeliporfin has now been granted and stipulates the risk eligibility criteria. Padeliporfin will be appraised within the population covered by its marketing authorisation

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Comparators	*Are these the standard treatments currently used in the NHS with which the technology should be compared?*		
	BAUS Section of Oncology	Yes	Comment noted. No changes to the scope are needed.
	Prostate Cancer UK	The comparators - active surveillance, radical surgery and radical radiotherapy - are appropriate to the stage of disease. Androgen deprivation therapy is not a relevant comparator as it is indicated for locally advanced prostate cancer.	Comment noted. No changes to the scope are needed.
	STEBA Biotech	Yes. All treatments should be considered with their subsequent re-treatments in case of disease progression (e.g., radical treatments following initial active surveillance)	Comment noted. No changes to the scope are needed.
Outcomes	*Will these outcome measures capture the most important health related benefits (and harms) of the technology?*		
	BAUS Section of Oncology	Yes	Comment noted. No changes to the scope are needed.
	Prostate Cancer UK	Yes	Comment noted. No changes to the scope are needed.
	STEBA Biotech	Additional outcomes to consider: • Absence of positive biopsy (as a measure of disease free survival)	Disease progression has been added to the outcomes. Particular measures of disease-

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		• Progression to Gleason pattern 4 or higher • Progression to PSA>10ng/mL over 3 consecutive measures • Progression to T3 clinical stage or higher • Progression outside of the eligibility criteria for TOOKAD® VTP treatment Maintenance of erectile and urinary functions could be considered outcomes	free survival or disease progression are not specified in the scope. Adverse events, including erectile dysfunction or incontinence, are included as outcomes.
Economic analysis	BAUS Section of Oncology	The time horizon in low to moderate risk needs to be long - probably around 10 years	Comment noted. No changes to the scope are needed.
	STEBA Biotech	The time horizon should encompass clinical progression and start of the next stage of therapies (e.g., radical treatment, ADT, chemotherapy)	Comment noted. No changes to the scope are needed.
Equality and Diversity	BAUS Section of Oncology	No issues	Noted.
	Prostate Cancer UK	The availability of padeliporfin for treating localised prostate cancer could reduce inequalities where radical surgery or radiotherapy is not provided as a treatment option. Padeliporfin could reduce age-based health inequalities in terms of access to active comparators. The Committee should consider evidence that shows men aged 80 or over have a statistically significant lower rate of access to surgery or radiotherapy compared to the England average. (Reference: Prostate Cancer UK. Men United vs Prostate Cancer: Five inequalities, five solutions. 2014. Available from: http://prostatecanceruk.org/media/2339836/inequalities-report.pdf).	Comment noted. If there is evidence that padeliporfin is a clinically effective treatment for people for whom alternative treatments may not be clinically suitable, or who may have lower rates of access to alternative treatments,

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			then please include this evidence in your submission. No changes to the scope are needed.
Innovation	*Do you consider the technology 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)?*		
	BAUS Section of Oncology	Yes	Comment noted. Please describe the innovative nature of padeliporfin in your submission to NICE. No changes to the scope are needed.
	Prostate Cancer UK	Yes. Padeliporfin is a potential 'step-change' in the management of localised prostate cancer because it offers a middle ground between the two extremes of active surveillance and radical surgery/radiotherapy. Padeliporfin potentially offers quality of life benefits over its comparators. The Appraisal Committee will be able to analyse phase III clinical trial data and draw comparisons with the known side-effects of radical surgery and radiotherapy.	Comment noted. Please describe the innovative nature of padeliporfin in your submission to NICE. No changes to the scope are needed.
Other considerations	BAUS Section of Oncology	It is very difficult to give advice when the methods by which we diagnose men is changing more quickly than the literature is able to reflect.	Comment noted. No changes to the scope are needed.

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Questions for consultation	BAUS Section of Oncology	No other questions	Noted.
	NCRI-ACP-RCP-RCR	*Questions for consultation* *In clinical practice, is it likely that padeliporfin will only be used for treating low-risk localised prostate cancer? Or is use in people with intermediate- and high-risk localised prostate cancer anticipated?* It will be difficult to recruit to a study that compares active surveillance with this new agent. There is an increasing trend for men who have low risk prostate cancer to be treated with active surveillance especially with increasing evidence for the use of MRI scanning to assess disease progression. Our experts believe that this new treatment may be better positioned as a comparator in the intermediate risk setting. *Have all relevant comparators for padeliporfin been included in the scope? Which treatments are considered to be established clinical practice in the NHS for localised prostate cancer? Which treatments would be expected to be displaced by photodynamic therapy?* Yes. Focal treatments may also be included. *Are androgen deprivation therapies relevant comparators for padeliporfin?* Androgen deprivation alone is used in men who are unsuitable for radical treatment options (surgery, radiotherapy etc) so may be considered in some cases as a comparator. *How should 'active surveillance' be defined?*	Comments noted. To reflect the population covered by the marketing authorisation, which has now been granted, this appraisal will consider specifically people with low-risk prostate cancer. NICE understands that the use of focal treatments for low-risk prostate cancer is not widespread in the NHS. Focal treatments have therefore not been added to the scope. NICE understands that androgen deprivation therapy is not established practice for low-risk disease, so is

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		The NICE protocol for active surveillance should be followed. *Have all relevant outcomes been included in the scope?* Biochemical progression free survival and Prostate-Specific Antigen (PSA) progression have not been included. *Are there any subgroups of people in whom padeliporfin is expected to be more clinically effective and cost effective or other groups that should be examined separately?* Our experts would be reluctant to consider its use in high risk prostate cancer without evidence of efficacy. *Where do you consider padeliporfin will fit into the existing NICE pathway, 'Prostate cancer'?* Intermediate risk localised prostate cancer *NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:* *Could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which padeliporfin will be licensed.* No	not included as a comparator. Disease progression has been added to the outcomes. Comment noted. The marketing authorisation has now been granted for padeliporfin which states it is indicated for low-risk prostate cancer. Comment noted.

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		Could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology. No *Could have any adverse impact on people with a particular disability or disabilities.* No *Do you consider padeliporfin 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)?* It is unlikely to produce a step change in low risk prostate cancer as there is currently debate whether these men should be treated at all.	Comments noted. Comment noted.
	STEBA Biotech	Androgen deprivation therapies are not relevant comparators for padeliporfin. Active surveillance could be defined as follow-up and care for UK patients with at least 10 year life-expectancy who do not undergo any radical treatment immediately after initial diagnosis. This will include among other items typical physician visits and tests that these UK patients receive. Padeliporfin might be more cost-effective in patients with unilateral disease at initial diagnosis	Comments noted. No further changes to the scope are needed.

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

Department of Health