National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Darolutamide with androgen deprivation therapy for treating non-metastatic hormone-relapsed 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
Wording	British Uro-oncology Group (BUG)	Yes	Comment noted. No action required.
	Janssen-Cilag Ltd UK	No comments.	Comment noted. No action required.
	TACKLE Prostate Cancer	Yes	Comment noted. No action required.
Timing Issues	British Uro-oncology Group (BUG)	Results of RCT published in NEJM in March 2019 showing significant PFS benefit. We need to issue an appraisal within the next 6 months	NICE has scheduled this topic into its work programme. For further details, see the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ta10476. No action required.

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	Janssen-Cilag Ltd UK	No comments.	Comment noted. No action required.
	TACKLE Prostate Cancer	NO COMMENT	Comment noted. No action required.
Additional comments on the draft remit	Bayer	No	Comment noted. No action required.
	British Uro-oncology Group (BUG)	It needs to include the latest published trial results	Comment noted. The remit should only include the technology and its proposed indication subject to appraisal. No action required.
	Janssen-Cilag Ltd UK	No comments.	Comment noted. No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Bayer	We suggest the following sentence is amended for more accuracy: Hormone-relapsed prostate cancer is diagnosed by rising prostate-specific antigen levels despite receiving androgen-deprivation therapy (ADT).	Comment noted. The sentence has been amended as suggested.

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	British Uro-oncology Group (BUG)	The addition of the ARAMIS phase 3 trial results is necessary	Comment noted. This section of the scope aims to provide a brief overview of the background for the appraisal. It is not intended to report the technology's pivotal trial results. These results will be presented by the company in its submission and will be considered by the committee at the time of the appraisal. No action required.
	Janssen-Cilag Ltd UK	No comments.	Comment noted. No action required.
	TACKLE Prostate Cancer	Good. The specific group of patients being targeted are a group that often greatly distressed by current treatment options – i.e. that drugs such as Abiraterone and Enzalutamide are not approved for use until metastases are demonstrated on conventional scanning techniques. *"Why are we waiting for the inevitable to happen before treatment is started?" "We know something is progressing –my PSA is rising. Whya am I not having anything done now?"*	Comment noted. No action required.
The technology/ intervention	Bayer	We suggest the following sentence is amended for more accuracy: Darolutamide plus ADT is being studied in a phase III trial, compared with placebo plus ADT, in adults with non-metastatic hormone-relapsed prostate cancer; with prostate-specific antigen levels of more than 2ng/ml.	Comment noted. The sentence has been amended as suggested.

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	British Uro-oncology Group (BUG)	Yes	Comment noted. No action required.
	Janssen-Cilag Ltd UK	No comments.	Comment noted. No action required.
	TACKLE Prostate Cancer	YES	Comment noted. No action required.
Population	Bayer	We agree that the population has been defined appropriately.	Comment noted. No action required.
	British Uro-oncology Group (BUG)	Yes	Comment noted. No action required.
	Janssen-Cilag Ltd UK	The pivotal phase 3 trial for darolutamide (ARAMIS) included patients who are at a high risk of developing metastatic disease (defined by a PSA doubling time of less than 10 months). Therefore, Janssen suggests that this is the relevant population to be considered separately in the scope.	Comment noted. PSA doubling time in the ARAMIS trial had a median of 4.4 months (range 0.7 to 11.0) and is not considered “high risk” as per NICE NG131 which defines the level of risk based on PSA level, Gleason score or clinical stage and not PSA doubling time. Subgroup analysis

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			by PSA doubling time has been added to the scope in response to British Uro-oncology Group (BUG)'s comment below on "other considerations". Clinical expert opinion will be sought during the appraisal on this. No action required.
	TACKLE Prostate Cancer	NO COMMENT	Comment noted. No action required.
Comparators	Bayer	Apalutamide with androgen deprivation therapy (subject to ongoing NICE appraisal) –Apalutamide is unlikely to be in use in the NHS at the time of the darolutamide appraisal and is therefore not an appropriate comparator.	Comment noted. The appraisal of apalutamide has now been suspended. It has been removed as a comparator in the scope
	British Uro-oncology Group (BUG)	Yes	Comment noted. The appraisal of apalutamide has now been suspended. It has been removed as a comparator in the scope

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	Janssen-Cilag Ltd UK	Janssen agrees that apalutamide with ADT is an appropriate comparator in this population (subject to ongoing NICE appraisal).	Comment noted. The appraisal of apalutamide has now been suspended. It has been removed as a comparator in the scope
	TACKLE Prostate Cancer	Abiraterone and Enzalutamide are not specifically mentioned but I assume are included under 'Androgen Deprivation Therapy'	Comment noted. Abiraterone is not licensed for this specific population, therefore cannot be considered an appropriate comparator. Enzalutamide has not been recommended by NICE and hence; is not considered an appropriate comparator to include. No action required.
Outcomes	Bayer	Yes	Comment noted. No action required.
	British Uro-oncology Group (BUG)	Yes	Comment noted. No action required.

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	Janssen-Cilag Ltd UK	No comments.	Comment noted. No action required.
	TACKLE Prostate Cancer	All of these are important to the patient.	Comment noted. No action required.
Economic analysis	Bayer	Bayer will be presenting a cost utility analysis over a time horizon sufficiently long to capture any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and PSS perspective.	Comment noted. No action required.
	British Uro-oncology Group (BUG)	Yes	Comment noted. No action required.
	Janssen-Cilag Ltd UK	No comments.	Comment noted. No action required.
	TACKLE Prostate Cancer	The cost of treatment is, to an extent, of secondary concern to the patient if the outcomes from treatment are significantly improved compared with current treatments.	Comment noted. The committee will consider costs alongside clinical effectiveness to ensure that any potential increase in costs is considered alongside improvement in outcomes. No action required.

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Equality and Diversity	Bayer	Bayer is not aware of any issues relating to inequalities.	Comment noted. No action required.
	British Uro-oncology Group (BUG)	Yes	Comment noted. No action required.
	Janssen-Cilag Ltd UK	No comments.	Comment noted. No action required.
	TACKLE Prostate Cancer	Although not strictly a standard 'equality' issue, patients are always aware that even when NICE Guidelines / Approval are issued, the ultimate decisions on offering treatments are often made at a local CCG level and considerably biased to cost issues. The term 'Postcode Lottery' is still a phrase still too commonly appropriate in some areas of the UK. There is also often a difference in availability of treatments in Scotland /Wales compared with England. This may not exactly be an 'Equality' issue as defined here, but is very important to patients scattered around the country.	Comment noted.. Potential inequalities in access to NICE recommended treatment will be noted. No action required.
Other considerations	Bayer	No additional issues have been identified.	Comment noted. No action required.
	British Uro-oncology Group (BUG)	Review evidence as per phase 3 trial and look at multivariate analysis to identify patient subgroup that would benefit the most based on PSA doubling time and patient characteristics.	Comment noted. The scope has been amended to include subgroup analysis by PSA doubling time if evidence allows.

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	Janssen-Cilag Ltd UK	No comments.	Comment noted. No action required.
	TACKLE Prostate Cancer	No Comment	Comment noted. No action required.
Innovation	Bayer	Darolutamide is a novel nonsteroidal androgen receptor (AR) inhibitor and Bayer considers that it is an innovative treatment option for non-metastatic castration resistant prostate cancer patients; darolutamide has the potential to increase the metastasis-free survival time. In preclinical studies, darolutamide demonstrated lower blood-brain barrier penetration compared to other currently available AR antagonists. There is an unmet need in this area since there are currently no other therapies approved by NICE for the treatment of this patient group.	Comments noted. Innovation will be considered by the appraisal committee when formulating its recommendations. No action required.
	British Uro-oncology Group (BUG)	Innovative. The improvement in disease free survival and quality of life free of interventions might not be reflected in the QALY calculation. The NEJM March 2019 publication and data on patient reported outcomes that the company could give.	Comments noted. Innovation will be considered by the appraisal committee when formulating its recommendations. No action required.
	Janssen-Cilag Ltd UK	No comments.	Comments noted. No action required.

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	TACKLE Prostate Cancer	It provides another alternative to the combined use of chemotherapy (docetaxel) and hormone therapy (ADT). There are other drugs undergoing a similar appraisal. It would seem inappropriate to exclude apalutamide from this overall process so that all alternatives can be appraised and the best alternative can be judged.	Comments noted. Innovation will be considered by the appraisal committee when formulating its recommendations. Apalutamide is included as a comparator. No action required.
Questions for consultation	Bayer	**Have all relevant comparators for darolutamide been included in the scope?** Apalutamide is unlikely to be in use in the NHS at the time of the darolutamide appraisal and is therefore not an appropriate comparator. Enzalutamide is not an appropriate comparator as it is not likely to be part of NHS clinical practice due to a negative recommendation from NICE. **Which treatments are considered established clinical practice in the NHS for non-metastatic hormone-relapsed prostate cancer?** No specific treatment although androgen deprivation therapy (ADT) would continue despite rising PSA. **Are the outcomes listed appropriate?** Bayer agrees with suggested outcome measures.	Comment noted. The appraisal of apalutamide has now been suspended. It has been removed as a comparator in the scope Comment noted. No action required. Comment noted. No action required.

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		Are there any subgroups of people in whom darolutamide is expected to be more clinically effective and cost effective or other groups that should be examined separately? Bayer agrees with the population as defined in the draft scope and have not identified any subgroups that should be examined separately. **Where do you consider darolutamide will fit into the existing NICE pathway, 'Prostate cancer'?** Managing relapse after radical treatment in patients with localised or locally advanced prostate cancer	Comment noted. No action required. Comment noted. No action required.
	British Uro-oncology Group (BUG)	Impact on performance status. Toxicity Profile.	Comment noted. "Impact on performance status" will be captured in the outcome "Health-related quality of life". Toxicity profile will be captured in the outcome "Adverse effects of treatment". No action required.
	Janssen-Cilag Ltd UK	No further comments.	Comment noted. No action required.

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	TACKLE Prostate Cancer	N/A	Comment noted. No action required.
Additional comments on the draft scope	Bayer	No additional comments.	Comment noted. No action required.
	Janssen-Cilag Ltd UK	No further comments.	Comment noted. No action required.

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

Department of Health and Social Care