National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Abemaciclib with fulvestrant for treating advanced hormone-receptor positive, HER2-negative breast cancer after endocrine therapy ID1339

Response to consultee and commentator 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

Section	Consultee/ Commentator	Comments [sic]	Action
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?*	Breast Cancer Now	Yes	No action required.
	Eli Lilly	No comments	No action required.
Timing Issues	Breast Cancer Now	As no appraisal for a CDK4/6 inhibitor with fulvestrant following endocrine therapy is currently active it would be helpful if this appraisal could be progressed quickly.	Comment noted. The dates of the expected marketing authorisation were taken into account when the topic was

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			planned into the work programme.
	Eli Lilly	Guidance close to marketing authorisation given an appropriate evidence base	Comment noted. The dates of the expected marketing authorisation were taken into account when the topic was planned into the work programme.
Additional comments on the draft remit	Eli Lilly	None	No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Breast Cancer Now	ONS cancer registration statistics for 2015 show that there were 9,626 deaths from breast cancer. The stats provided for 5 year survival rates for metastatic breast cancer and percentage people with early or locally advanced breast cancer progressing to metastatic breast cancer are local rather than national statistics, as the document suggests. Although fulvestrant is not recommended by NICE for use following endocrine therapy, it is routinely available in some local areas following confirmation that it was 'in tariff' when it was removed from the Cancer Drugs Fund.	Thank you for your comments. The background section has been updated in the final scope. Fulvestrant is included in the list of comparators in the scope.

Section	Consultee/ Commentator	Comments [sic]	Action
	Eli Lilly	No comments	No action required.
The technology/ intervention *Is the description of the technology or technologies accurate?*	Breast Cancer Now	To the best of our knowledge.	No action required.
	Eli Lilly	Yes	No action required.
Population *Is the population defined appropriately? Are there groups within this population that should be considered separately?*	AstraZeneca	In the pivotal study - MONARCH2 – a difference in efficacy was observed in pre- and post menopausal patients which may suggest these patients could be considered separately.	Thank you for your comment. All pre- or perimenopausal women received a gonadotropin-releasing hormone agonist. The company could make a case for a sub-group if they choose. No change required to scope.
	Breast Cancer Now	Yes. We are not aware of any groups that should be considered separately.	No action required.
	Eli Lilly	Please note that the draft label proposes that abemaciclib is used in combination with [redacted], or following endocrine therapy. We would anticipate that the proposed comparator set remains the same for both populations.	Thank you for your comments. The population has been updated in the final scope.

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	Pfizer	The draft scope words the population as: "People with advanced hormone-receptor positive HER2-negative breast cancer that has progressed after endocrine therapy." For this population, it is important to distinguish when patients have progressed after endocrine therapy, i.e. at what stage progression occurred. • Patients who successfully complete endocrine therapy in the adjuvant setting would be expected to be given endocrine therapy as a first-line metastatic treatment option. If patients' disease then progresses on a first-line endocrine therapy in the metastatic setting, abemaciclib in combination with fulvestrant may be an appropriate treatment (i.e. as a second-line therapy in the metastatic setting). These patients are thus relevant to this appraisal. • However, another population relevant for this appraisal are those who did not successfully complete endocrine therapy in the adjuvant and the neoadjuvant setting (i.e. disease advanced before the end of, or soon after, adjuvant or neoadjuvant treatment), and then present for first-line treatment in the metastatic setting. Due to the limited success of adjuvant or neoadjuvant endocrine therapy in these patients, abemaciclib plus fulvestrant could be considered as a first-line treatment option in the metastatic setting for these patients. The population is correctly worded in that abemaciclib plus fulvestrant is a treatment option for disease which has progressed after endocrine therapy, but it is important to note that this may include after first-line metastatic endocrine therapy (i.e. as a second-line metastatic treatment option), but also directly after adjuvant or neoadjuvant endocrine therapy (i.e. as a first-line metastatic treatment option).	Comment noted. The population has been updated in the final scope.

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Comparators *Is this (are these) the standard treatment(s) currently used in the NHS with which the technology should be compared? Can this (one of these) be described as 'best alternative care'?*	Breast Cancer Now	Yes	No action required.
	Eli Lilly	We do not believe tamoxifen should be a comparator. The NICE pathway does not reference treatment with tamoxifen for patients who have progressed following prior endocrine therapy. Additionally, chemotherapy should not be included as a comparator. TA421 (Everolimus with exemestane for treating advanced breast cancer after endocrine therapy) made no comparison with chemotherapy and the recommendation was based on a comparison with exemestane alone. Nor was chemotherapy a comparator in TA259 (Fulvestrant).	Comment noted. CG81 recommends chemotherapy on disease progression and endocrine therapy is offered to people who were treated with chemotherapy first line. No changes to scope needed.
Outcomes *Will these outcome measures capture the most important health related benefits (and harms) of the technology?*	Breast Cancer Now	Yes	No action required.
	Eli Lilly	We agree with the outcome measures stated	No action required.
Economic analysis	Eli Lilly	It is anticipated that a lifetime horizon will be considered.	Comment noted. No action required.
Equality and Diversity	Eli Lilly	No issues identified.	No action required.
Other considerations	Eli Lilly	No comments	No action required.

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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)?*	AstraZeneca	No. Abemaciclib is one of three CDK 4/6 inhibitors in this class of molecules.	Comment noted. No action required.
	Breast Cancer Now	The class of medicines to which abemaciclib belongs is considered to be innovative. Clincial trial data suggests abemacicilb and fulvestrant significantly extends progression free survival compared to fulvestrant alone.	Comment noted. The innovative nature of abemaciclib will be considered by the committee during the appraisal.
	Eli Lilly	Abemaciclib is anticipated to be the first CDK 4/6 inhibitor to allow continuous dosing. This may present advantages to patients with respect to compliance and ease of use of the treatment. This aspect may be captured in the time on treatment data available but aspects that are less easy to quantify, such as fewer missed doses due to the simpler dosing regimen should be considered.	Comment noted. The innovative nature of abemaciclib will be considered by the committee during the appraisal.
Questions for consultation	AstraZeneca	Appropriateness of the cost comparison methodology to this topic. Abemaciclib is the third member of this class of molecules (CDK 4/6 inhibitors) and is likely to be similar in its clinical efficacy and resource use to palbociclib in this setting. The primary outcome measured in the study is still clinically relevant.	Comment noted.
	Eli Lilly	We expect abemaciclib plus fulvestrant to be a treatment option alongside the other second-line treatments noted in the NICE treatment pathway- everolimus and fulvestrant.	Comment noted. No action required.

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Additional comments on the draft scope	AstraZeneca	The relevance of NICE TA423 to this appraisal is unclear given it relates to treatment following 2 or more chemotherapy regimens.	Comment noted. The related NICE guidance section has been updated in the final scope.
	Eli Lilly	No further comments	No action required.
	Novartis	For awareness Novartis have a clinical trial in the same population, MONALEESA-3, which are expecting to report [redacted], however this study is event driven.	Comment noted. No action required.

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

None.