NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

SINGLE TECHNOLOGY APPRAISAL

Abemaciclib with an aromatase inhibitor for untreated advanced hormone-receptor positive, HER2-negative breast cancer [ID1227]

The following documents are made available to the consultees and commentators:

1. **Response to consultee, commentator and public comments on the Appraisal Consultation Document (ACD)**

2. **Consultee and commentator comments on the Appraisal Consultation Document** from:

    - Eli Lilly and Company
    - Breast Cancer Now
    - UK Breast Cancer
    - Pfizer

Any information supplied to NICE which has been marked as confidential, has been redacted. All personal information has also been redacted.

Appraisal title

Single Technology Appraisal

Response to consultee, commentator and public comments on the Appraisal Consultation Document (ACD)

Type of stakeholder:

Consultees – Organisations that accept an invitation to participate in the appraisal including the companies, national professional organisations, national patient organisations, the Department of Health and Social Care and the Welsh Government and relevant NHS organisations in England. Consultees can make a submission and participate in the consultation on the appraisal consultation document (ACD; if produced). All non-company consultees can nominate clinical experts and/or patient experts to verbally present their personal views to the Appraisal Committee. Company consultees can also nominate clinical experts. Representatives from NHS England and clinical commissioning groups invited to participate in the appraisal may also attend the Appraisal Committee as NHS commissioning experts. All consultees have the opportunity to consider an appeal against the final recommendations, or report any factual errors, within the final appraisal document (FAD).

Clinical and patient experts and NHS commissioning experts – The Chair of the Appraisal Committee and the NICE project team select clinical experts and patient experts from nominations by consultees and commentators. They attend the Appraisal Committee meeting as individuals to answer questions to help clarify issues about the submitted evidence and to provide their views and experiences of the technology and/or condition. Before they attend the meeting, all experts must either submit a written statement (using a template) or indicate they agree with the submission made by their nominating organisation..

Commentators – Commentators can participate in the consultation on the ACD (if produced), but NICE does not ask them to make any submission for the appraisal. Non-company commentator organisations can nominate clinical experts and patient experts to verbally present their personal views to the Appraisal Committee. Commentator organisations representing relevant comparator technology companies can also nominate clinical experts. These organisations receive the FAD and have opportunity to report any factual errors. These organisations include comparator technology companies, Healthcare Improvement Scotland any relevant National Collaborating Centre (a group commissioned by NICE to develop clinical guidelines), other related research groups where appropriate (for example, the Medical Research Council and National Cancer Research Institute); other groups such as the NHS Confederation, the NHS Commercial Medicines Unit, the Scottish Medicines Consortium, the Medicines and Healthcare Products Regulatory Agency, the Department of Health and Social Care, Social Services and Public Safety for Northern Ireland).

Public – Members of the public have the opportunity to comment on the ACD when it is posted on the Institute's web site 5 days after it is sent to consultees and commentators. These comments are usually presented to the appraisal committee in full, but NICE reserves the right to summarise and edit comments received during consultations, or not to publish them at all, where in the reasonable opinion of NICE, the comments are voluminous, publication would be unlawful or publication would be otherwise inappropriate.

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 number	Type of stakeholder	Organisation name	Stakeholder comment Please insert each new comment in a new row	NICE Response Please respond to each comment
1	Patient group	Breast Cancer Now	Abemaciclib does have a slightly different side effect profile to the other treatment options that have recently become standard of care – both palbociclib and ribociclib in combination with an aromatase inhibitor. Palbociclib and ribociclib are associated with an increased incidence of neutropenia, whereas abemaciclib is linked with an increased likelihood of diarrhoea, although this can often be managed with medication and is more common when starting the treatment. With a slightly different side effect profile, abemaciclib with an aromatase inhibitor could provide an alternative treatment option that may be preferred by some patients. The side effect profile of drugs is an important factor for many patients in their treatment decisions and if abemaciclib was recommended for use it would expand the options available for clinicians to discuss with their patients.	Thank you for your comments. Abemaciclib with an aromatase inhibitor is now recommended for hormone-receptor positive, HER2-negative, locally advanced or metastatic breast cancer previously untreated in the advanced setting (see FAD section 1.1 for more details).
2	Patient group	UK Breast Cancer Group	Abemaciclib is a CDK4/6 inhibitor which when combined with an aromatase inhibitor results in prolonged progression-free survival with acceptable toxicity. It has similar efficacy but different toxicity to two other CDK4/6 inhibitors, palbociclib and ribociclib, that have already been approved for use in the NHS by NICE. On behalf of the the UKBCG we would like to express our dissatisfaction with this guidance that removes an option of therapy from patients and their physicians that is effective and well-tolerated. We hope that the Committee will reconsider their decision.	Thank you for your comments. Abemaciclib with an aromatase inhibitor is now recommended for hormone-receptor positive, HER2-negative, locally advanced or metastatic breast cancer previously untreated in the advanced setting (see FAD section 1.1 for more details).
3	Company	Lilly	Lilly would like to thank NICE for their appraisal and the opportunity to comment on the appraisal consultation document (ACD) for ID1227. Lilly are naturally disappointed that NICE has not recommended abemaciclib with an aromatase inhibitor (AI), within its anticipated marketing authorisation, as an option for treating women with locally advanced or metastatic, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer as initial endocrine-based therapy. However, we are pleased that there is considerable agreement between Lilly and the committee at this stage, in that abemaciclib with an AI shows improved progression-free survival compared to an AI alone, which would be highly valued by patients and their families. Lilly also agree that the three cyclin-dependent kinase 4 and 6 (CDK4 & 6) inhibitors (abemaciclib, palbociclib, ribociclib) have similar clinical effectiveness, with some differences noted in their respective safety profiles. Lilly agree that a cost-comparison approach is appropriate for abemaciclib, palbociclib and ribociclib. Given there are no differences to model following the	Thank you for your comments. Abemaciclib with an aromatase inhibitor is now recommended for hormone-receptor positive, HER2-negative, locally advanced or metastatic breast cancer previously untreated in the advanced setting (see FAD section 1.1 for more details).

Comment number	Type of stakeholder	Organisation name	Stakeholder comment Please insert each new comment in a new row	NICE Response Please respond to each comment
			committee's ACD conclusions on the cost-effectiveness estimates, we propose that a simple comparison of the patient access scheme (PAS) prices of the three CDK4 & 6 inhibitors should be conducted. In light of this, Lilly are offering a revised PAS price for abemaciclib of [redacted] (a discount of [redacted] from list). We look forward to hearing from you following our provision of this revised PAS price. Please do not hesitate to contact me if you have any further queries.	
4	Commentator	Pfizer Ltd	There are similarities in observed efficacy across the 3 targeted inhibitors – abemaciclib, palbociclib and ribociclib – with the submitting manufacturer for abemaciclib concluding comparability from their network meta-analysis: "the treatment effects for each of the endpoints were similar between ABE-ANAS/LTZ, PAL-ANAS/LTZ and RIBO-ANAS/LTZ, supporting that the efficacy of abemaciclib plus NSAI is at a minimum comparable to ribociclib or palbociclib plus NSAI (letrozole)". Pfizer is not aware of evidence that would support an assumed efficacy advantage for abemaciclib versus either palbociclib or ribociclib combined with an aromatase inhibitor. Indeed, the committee concluded that an assumption of comparability is preferred between the inhibitors (ACD 3.13). Noting the above consensus that abemaciclib does not appear to be associated with superior efficacy versus either palbociclib or ribociclib, the company's economic model appears contradictory as it produced a QALY advantage for abemaciclib over palbociclib and ribociclib; the robustness of economic model results that favour abemaciclib thus appear questionable. Any incremental cost difference modelled for abemaciclib (outside of the acquisition cost of drug) is similarly questionable. With consensus that abemaciclib does not appear to be associated with superior efficacy to palbociclib or ribociclib, Pfizer acknowledge the committee's preference for a cost-comparison approach. A significant amount of the direct and indirect, clinical and economic evidence is redacted which has hindered Pfizer's ability to comment in more detail.	Thank you for your comments. The committee did not see any compelling evidence of differing efficacy and considered the cost of the 3 targeted inhibitors – abemaciclib, palbociclib and ribociclib directly (see FAD section 3.14 for more details). Abemaciclib with an aromatase inhibitor is now recommended for hormone-receptor positive, HER2-negative, locally advanced or metastatic breast cancer previously untreated in the advanced setting (see FAD section 1.1 for more details).

Eli Lilly and Company Limited

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National Institute for Health and Care Excellence
10 Spring Gardens
London
SW1A 2BU
United Kingdom

8th November 2018

RE: Lilly response to ACD: abemaciclib with an aromatase inhibitor for previously untreated, hormone-receptor positive, HER2-negative, locally advanced or metastatic breast cancer [ID1227]

Dear Helen Knight,

Lilly would like to thank NICE for their appraisal and the opportunity to comment on the appraisal consultation document (ACD) for ID1227.

Lilly are naturally disappointed that NICE has not recommended abemaciclib with an aromatase inhibitor (AI), within its anticipated marketing authorisation, as an option for treating women with locally advanced or metastatic, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer as initial endocrine-based therapy. However, we are pleased that there is considerable agreement between Lilly and the committee at this stage, in that abemaciclib with an AI shows improved progression-free survival compared to an AI alone, which would be highly valued by patients and their families. Lilly also agree that the three cyclin-dependent kinase 4 and 6 (CDK4 & 6) inhibitors (abemaciclib, palbociclib, ribociclib) have similar clinical effectiveness, with some differences noted in their respective safety profiles.

Lilly agree that a cost-comparison approach is appropriate for abemaciclib, palbociclib and ribociclib. Given there are no differences to model following the committee's ACD conclusions on the cost-effectiveness estimates, we propose that a simple comparison of the patient access scheme (PAS) prices of the three CDK4 & 6 inhibitors should be conducted. In light of this, Lilly are offering a revised PAS price for abemaciclib of £[redacted] (a discount of [redacted] from list).

We look forward to hearing from you following our provision of this revised PAS price. Please do not hesitate to contact me if you have any further queries.

Yours sincerely,

XXXXXXXX XXXXXXXXX

Head of Health Outcomes & HTA, Lilly UK

NICE National Institute for Health and Care Excellence

Abemaciclib with an aromatase inhibitor for untreated advanced hormone-receptor positive, HER2-negative breast cancer [ID1227]

Consultation on the appraisal consultation document – deadline for comments 5pm on 08/11/2018 **return comments to:** NICE DOCS

	Please read the checklist for submitting comments at the end of this form. We cannot accept forms that are not filled in correctly. The Appraisal Committee is interested in receiving comments on the following: • has all of the relevant evidence been taken into account? • are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence? • are the provisional recommendations sound and a suitable basis for guidance to the NHS? 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 preliminary recommendations may need changing in order to meet these aims. In particular, please tell us if the preliminary recommendations: • could have a different impact on people protected by the equality legislation than on the wider population, for example by making it more difficult in practice for a specific group to access the technology; • could have any adverse impact on people with a particular disability or disabilities. Please provide any relevant information or data you have regarding such impacts and how they could be avoided or reduced**.**
Organisation name – Stakeholder or respondent (if you are responding as an individual rather than a registered stakeholder please leave blank):	Breast Cancer Now
Disclosure Please disclose any past or current, direct or indirect links to, or funding from, the tobacco industry.	None
Name of commentator person completing form:	[redacted]

Comment number	Comments

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	Insert each comment in a new row. Do not paste other tables into this table, because your comments could get lost – type directly into this table.
1	It is disappointing that NICE has not been able to recommend abemaciclib with an aromatase inhibitor as an option for treating locally advanced or metastatic, hormone receptor-positive, HER2-negative breast cancer. We note that abemaciclib with an aromatase inhibitor has not been recommended by NICE as it is not considered a cost-effective use of NHS resources. We recognise that the base-case analyses using the patient access schemes for all 3 CDK 4/6 inhibitors suggests that the ICERs for abemaciclib are significantly higher than £30,000 per QALY gained. We would urge Eli Lilly to work with NICE and NHS England to see if the cost-effectiveness of abemaciclib with an aromatase inhibitor could be improved in order to enable NICE to recommend it for use.
2	Abemaciclib does have a slightly different side effect profile to the other treatment options that have recently become standard of care – both palbociclib and ribociclib in combination with an aromatase inhibitor. Palbociclib and ribociclib are associated with an increased incidence of neutropenia, whereas abemaciclib is linked with an increased likelihood of diarrhoea, although this can often be managed with medication and is more common when starting the treatment. With a slightly different side effect profile, abemaciclib with an aromatase inhibitor could provide an alternative treatment option that may be preferred by some patients. The side effect profile of drugs is an important factor for many patients in their treatment decisions and if abemaciclib was recommended for use it would expand the options available for clinicians to discuss with their patients.
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Insert extra rows as needed

Checklist for submitting comments

- Use this comment form and submit it as a Word document (not a PDF).
- Complete the disclosure about links with, or funding from, the tobacco industry.
- Combine all comments from your organisation into 1 response. We cannot accept more than 1 set of comments from each organisation.
- Do not paste other tables into this table – type directly into the table.
- Please underline all confidential information, and separately highlight information that is submitted under 'commercial in confidence' in turquoise and all information submitted under 'academic in confidence' in yellow. If confidential information is submitted, please also send a 2nd version of your comment with that information replaced with the following text: 'academic / commercial in confidence information removed'. See the Guide to the processes of technology appraisal (section 3.1.23 to 3.1.29) for more information.
- Do not include medical information about yourself or another person from which you or the person could be identified.
- Do not use abbreviations
- Do not include attachments such as research articles, letters or leaflets. For copyright reasons, we will have to return comments forms that have attachments without reading them. You can resubmit your comments form without attachments, it must send it by the deadline.

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Organisation name – Stakeholder or respondent (if you are responding as an individual rather than a registered stakeholder please leave blank):	[**IUK Breast Cancer Group**]
Disclosure Please disclose any past or current, direct or indirect links to, or funding from, the tobacco industry.	[**I have attended a paid advisory Board with Lilly for Abemaciclib on the 5th October 2018**]
Name of commentator person completing form:	XXXXXXXX XXXXXXXX

Comment number	Comments

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Example 1	We are concerned that this recommendation may imply that ……..
1	Abemaciclib is a CDK4/6 inhibitor which when combined with an aromatase inhibitor results in prolonged progression-free survival with acceptable toxicity. It has similar efficacy but different toxicity to two other CDK4/6 inhibitors, palbociclib and ribociclib, that have already been approved for use in the NHS by NICE. On behalf of the the UKBCG we would like to express our dissatisfaction with this guidance that removes an option of therapy from patients and their physicians that is effective and well-tolerated. We hope that the Committee will reconsider their decision.
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Organisation name – Stakeholder or respondent (if you are responding as an individual rather than a registered stakeholder please leave blank):	Pfizer Ltd
Disclosure Please disclose any past or current, direct or indirect links to, or funding from, the tobacco industry.	None
Name of commentator person completing form:	[redacted]

Comment number	Comments

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	There are similarities in observed efficacy across the 3 targeted inhibitors – abemaciclib, palbociclib and ribociclib – with the submitting manufacturer for abemaciclib concluding comparability from their network meta-analysis: *"the treatment effects for each of the **endpoints were similar** between ABE-ANAS/LTZ, PAL-ANAS/LTZ and RIBO-ANAS/LTZ, supporting that the efficacy of abemaciclib plus NSAI is at a minimum **comparable to ribociclib or palbociclib** plus NSAI (letrozole)".* Pfizer is not aware of evidence that would support an assumed efficacy advantage for abemaciclib versus either palbociclib or ribociclib combined with an aromatase inhibitor. Indeed, the committee concluded that an assumption of comparability is preferred between the inhibitors (ACD 3.13). Noting the above consensus that abemaciclib does not appear to be associated with superior efficacy versus either palbociclib or ribociclib, the company's economic model appears contradictory as it produced a QALY advantage for abemaciclib over palbociclib and ribociclib; the robustness of economic model results that favour abemaciclib thus appear questionable. Any incremental cost difference modelled for abemaciclib (outside of the acquisition cost of drug) is similarly questionable. With consensus that abemaciclib does not appear to be associated with superior efficacy to palbociclib or ribociclib, Pfizer acknowledge the committee's preference for a cost-comparison approach. A significant amount of the direct and indirect, clinical and economic evidence is redacted which has hindered Pfizer's ability to comment in more detail.

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