National Institute for Health and Care Excellence

Health Technology Evaluation

Imlunestrant for treating oestrogen receptor-positive HER2-negative advanced breast cancer after endocrine therapy ID6373
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	Eli Lilly	No comments. Lilly agrees that the proposed single technology appraisal is the most appropriate evaluation route for imlunestrant	No action required.
	Breast Cancer Now	Yes, it is appropriate to evaluate the technology through a single technology appraisal	No action required.
	METUPUK	The topic is suitable for evaluation as a STA	No action required.
Wording	Eli Lilly	No comments	No action required.
	Breast Cancer Now	Yes	No action required.
	METUPUK	Yes although if the marketing authorisation is restricted to patients with alterations in ESR1, then this should be reflected in the wording of the remit	Thank you for your comment. The wording of the remit is kept broad in the scope.

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			Imlunestrant will be appraised within its marketing authorisation. No action required.
Additional comments on the draft remit	Eli Lilly	N/A – no additional comments	No action required.
	Breast Cancer Now	[None]	No action required.
	METUPUK	[None]	No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Eli Lilly	No comments	No action required.
	Breast Cancer Now	We consider this information to be accurate and complete	No action required.
	METUPUK	No comments	No action required.
Population	Eli Lilly	The draft scope is accurate, no amendments are required	No action required.
	Breast Cancer Now	The population is defined as 'People with oestrogen receptor-positive, HER2-negative locally advanced or metastatic breast cancer after endocrine treatment'. At this stage in their treatment most patients would have already been treated with a CDK4/6 inhibitor in addition to endocrine treatment	Thank you for your comment. The population is kept broad in the scope. Imlunestrant will be

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			appraised within its marketing authorisation. No action required.
	METUPUK	Yes	No action required.
Subgroups	Eli Lilly	The draft scope is accurate, no amendments are required	No action required.
	Breast Cancer Now	We understand that the Ember-4 phase 3 [trial] considered patients both with and without an ESR1 mutation, as a result it may be appropriate to consider patients with an ESR1 mutation as a sub-group within the population	Thank you for your comment. The scope has been updated to include the subgroup with an ESR1 mutation detected.
	METUPUK	Patients with an ESR1 mutation, as suggested in the scope	Thank you for your comment. The scope has been updated to include the subgroup with an ESR1 mutation detected.
Comparators	Eli Lilly	The draft scope is accurate, no amendments are required	No action required
	Breast Cancer Now	Yes. We would note that capivasertib is currently listed as a single agent comparator, (subject to appraisal). We understand that the scope for the appraisal of capivasertib proposed that it would be considered in combination with fulvestrant	Thank you for your comment. The scope has been updated to include fulvestrant given in combination with capivasertib as a possible comparator.

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	METUPUK	No comments, clinical input is more appropriate in this section	No action required.
Outcomes	Eli Lilly	The draft scope is accurate, no amendments are required	No action required.
	Breast Cancer Now	Yes	No action required.
	METUPUK	Yes the listed outcomes are appropriate	No action required.
Equality	Eli Lilly	No equality issues were identified	No action required.
	Breast Cancer Now	No comments	No action required.
	METUPUK	None noted	No action required.
Other considerations	Eli Lilly	No comments	No action required.
	Breast Cancer Now	No further comments	No action required.
	METUPUK	No comments	No action required.
Questions for consultation [questions shown in italics]	Eli Lilly	*Where do you consider imlunestrant will fit into the existing care pathway for oestrogen receptor-positive, HER2-negative advanced breast cancer?* Based on the characteristics of patients in EMBER3, the potential placements of imlunestrant could be as: • first-line treatment for people who have relapsed while on or within 12 months of completion of (neo)adjuvant aromatase	Thank you for your comment. The background section of the scope has been updated to include that people could have had

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		inhibitor, alone or in combination with a CDK4/6 inhibitor, with no treatment for advanced disease. • second-line treatment for people who have relapsed more than 12 months from completion of (neo)adjuvant endocrine therapy with subsequent progression on or after only 1 line of therapy with an aromatase inhibitor, alone or in combination with a CDK4/6 inhibitor. • second-line treatment for people with de novo metastatic disease, with subsequent progression on or after only 1 line of therapy with an aromatase inhibitor, alone or in combination with a CDK4/6 inhibitor.	surgery for early and locally advanced disease as a previous treatment.
		The clinical trial studied imlunestrant with or without abemaciclib. If permitted within the final marketing authorisation, will imlunestrant be used both with and without abemaciclib? Are there clearly defined clinical populations who would expected to receive imlunestrant as monotherapy or in combination with abemaciclib? Imlunestrant is anticipated to be used either with or without abemaciclib. Based on current clinical practice and treatment guidelines in the UK, it may be appropriate for imlunestrant monotherapy and imlunestrant in combination with abemaciclib to be used at different stages in the treatment pathway.	Thank you for your comment. The intervention specifies imlunestrant with or without abemaciclib. Subgroups according to positions in the pathway can be explored in the company's evidence submission if appropriate.
		The phase 3 trial of imlunestrant with or without abemaciclib for the treatment of patients with oestrogen receptor-positive, HER2- advanced breast cancer considers outcomes in all patients and patients with detectable ESR1 mutations. Are ESR1 mutations routinely tested for in	Thank you for your comments. The scope has been updated to

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		oestrogen receptor-positive, HER2-negative advanced breast cancer in NHS practice? ESR1 mutations are not routinely tested in NHS practice. *Are there any subgroups of people in whom imlunestrant with or without abemaciclib is expected to be more clinically effective and cost effective? In particular, should the subgroup of patients with mutations in ESR1 be examined separately?* As per the pre-specified analysis of EMBER3, relevant subgroups of interest including patients with mutations in ESR1 will be assessed within the scope of the submission. No specific subgroups of interest were identified in the draft scope. *Have all relevant comparators for imlunestrant with or without abemaciclib been included in the scope?* The draft scope is accurate, no amendments are required with regards to relevant comparators. *Would imlunestrant with or without abemaciclib be a candidate for managed access?* The comparative efficacy data to be presented in this submission are anticipated to be suitably robust to allow imlunestrant with or without abemaciclib to be considered for routine commissioning. However, should NICE deem that a managed access agreement may be more appropriate for imlunestrant with or without abemaciclib in this	include the need for costing of ESR1 mutation diagnosis in the economic model if testing is needed. Thank you for your comment. Subgroups according to ESR1 mutation has been added to the scope. No action required. No action required.

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		indication, future additional data is expected to become available, although the time of data availability is currently uncertain.	
		Do you consider that the use of imlunestrant with or without abemaciclib can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits. No comments.	No action required.
		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 imlunestrant with or without abemaciclib will be licensed;* • *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;* • *could have any adverse impact on people with a particular disability or disabilities.* *Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.*	No action required.

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		No issues identified.	
	Breast Cancer Now	*Where do you consider imlunestrant will fit into the existing care pathway for oestrogen receptor-positive, HER2-negative advanced breast cancer?* This treatment is currently being studied in a clinical trial compared with endocrine therapy. Most patients with ER-positive, HER2 negative secondary breast cancer will start treatment with endocrine therapy in the form of an aromatase inhibitor (anastrazole, exemestane or letrozole) alongside a CDK4/6 inhibitor (abemaciclib, ribociclib or palbociclib). The draft scope indicates that imlunestrant could be used as a second line treatment after endocrine therapy.	No action required.
		The clinical trial studied imlunestrant with or without abemaciclib. If permitted within the final marketing authorisation, will imlunestrant be used both with and without abemaciclib? Are there clearly defined clinical populations who would expected to receive imlunestrant as monotherapy or in combination with abemaciclib? Published results for the clinical trial do not appear to be available so it is difficult for us to comment on this. Most patients will receive a CDK4/6 inhibitor as part of their first line treatment, which could be abemaciclib. We would anticipate that patients who have received abemaciclib as part of first line treatment would not be offered it as part of second line treatment.	No action required.
		The phase 3 trial of imlunestrant with or without abemaciclib for the treatment of patients with oestrogen receptor-positive, HER2- advanced breast cancer considers outcomes in all patients and patients with detectable ESR1 mutations. Are ESR1 mutations routinely tested for in	Thank you for your comments. The scope has been updated to include the need for

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		oestrogen receptor-positive, HER2-negative advanced breast cancer in NHS practice? Our understanding is that ESR1 is not routinely tested for on the NHS. ESR1 testing is likely to be considered as part of the ongoing technology appraisal of elacestrant or treating oestrogen receptor-positive, HER2-negative advanced breast cancer with an ESR1 mutation after at least 1 endocrine treatment (GID-TA11263). *Are there any subgroups of people in whom imlunestrant with or without abemaciclib is expected to be more clinically effective and cost effective? In particular, should the subgroup of patients with mutations in ESR1 be examined separately?* Published results for the phase 3 clinical trial do not appear to be available so it is difficult for us to comment on this. *Have all relevant comparators for imlunestrant with or without abemaciclib been included in the scope?* Yes, to the best of our knowledge *Would imlunestrant with or without abemaciclib be a candidate for managed access?* Yes	costing of ESR1 mutation diagnosis in the economic model if testing is needed. No action required. No action required. No action required.

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		Do you consider that the use of imlunestrant with or without abemaciclib can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? Not known *Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.* N/A	No action required. No action required.
	METUPUK	*Are ESR1 mutations routinely tested for in oestrogen receptor-positive, HER2-negative advanced breast cancer in NHS practice?* ESR1 testing is not currently carried out in routine NHS practice upon progression. If ESR1 testing is to be used, will a ctDNA method be used? *If permitted within the final marketing authorisation, will imlunestrant be used both with and without abemaciclib? Are there clearly defined clinical populations who would expected to receive imlunestrant as monotherapy or in combination with abemaciclib?* If imunlestrant and abemaciclib is considered, will patients who have prior treatment with abemaciclib be excluded? If there is exclusion, will this refer to abemaciclib in the metastatic setting only, or in both the early and metastatic setting?	Thank you for your comments. The scope has been updated to include the need for costing of ESR1 mutation diagnosis in the economic model if testing is needed. Thank you for your comments. Imlunestrant will be appraised within its marketing authorisation and will be guided by the evidence base. Clinical expert

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			advice on the place of imlunestrant with and without abemaciclib in the treatment pathway for advanced breast cancer will be obtained during the appraisal. No action required.
Additional comments on the draft scope	Eli Lilly	[None]	No action required.
	Breast Cancer Now	[None]	No action required.
	METUPUK	[None]	No action required.

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

Making Seconds Count