

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Imlunestrant for treating oestrogen receptor-positive HER2-negative advanced breast cancer after endocrine therapy

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of imlunestrant within its marketing authorisation for treating oestrogen receptor-positive, HER2-negative advanced breast cancer after endocrine treatment.

Background

Breast cancer arises from the tissues of the ducts or lobules of the breast. The cancer is said to be 'advanced' if it has spread to other parts of the body such as the bones, liver, and lungs (metastatic cancer), or if it has grown directly into nearby tissues and cannot be completely removed by surgery.

In 2021 in England, 49,775 people were diagnosed with breast cancer.¹ Approximately 12.7% of people with breast cancer in England in 2021 had advanced stage disease (stage III or IV) when they were diagnosed.^{1,2} The 1-year survival rate for adults diagnosed at stage IV (metastatic breast cancer) in England is 67%.² Around 35% of people with early or locally advanced disease will progress to metastatic breast cancer in the 10 years following diagnosis.³

Current treatments for advanced breast cancer aim to relieve symptoms, prolong survival and maintain a good quality of life with minimal adverse events. Treatment depends on whether the cancer cells have particular receptors, the extent of the disease, and previous treatments. The most prevalent type of breast cancer is hormone receptor-positive, human epidermal growth factor receptor 2 (HER2)-negative disease.⁴ Oestrogen receptor-positive breast cancer is a type of hormone receptor-positive disease. Oestrogen receptor 1 (ESR1) mutations develop in 20% to 40% of people with metastatic breast cancer after treatment with an aromatase inhibitor.⁵ An aromatase inhibitor is a type of endocrine therapy.

NICE technology appraisals [495](#), [496](#) and [563](#) recommend use of an aromatase inhibitor in combination with cyclin-dependent kinase 4 and 6 (CDK 4/6) inhibitors (palbociclib, ribociclib and abemaciclib respectively) for treating hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer as initial endocrine-based therapy in adults.

- The choice of endocrine therapy is guided by [NICE clinical guideline 81](#) (CG81). In people who have been through the menopause, endocrine therapies include non-steroidal aromatase inhibitors (anastrozole and letrozole) or tamoxifen, if aromatase inhibitors are not tolerated or are contraindicated. People who are before menopause or around menopause will have first-line treatment with tamoxifen and ovarian suppression if they have not previously received tamoxifen. Men may receive tamoxifen as a first-line endocrine treatment.

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- For people whose disease is life-threatening or requires early relief of symptoms, CG81 recommends chemotherapy first, followed by endocrine therapy.

For people whose hormone receptor-positive, HER2-negative advanced breast cancer has recurred or progressed after a non-steroidal aromatase inhibitor:

- NICE technology appraisal [421](#) recommends treatment with everolimus plus exemestane.
- NICE technology appraisals [687](#), [725](#) and [836](#) recommend abemaciclib, ribociclib and palbociclib, all in combination with fulvestrant, for treating hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer in people who have had previous endocrine therapy and only if, exemestane plus everolimus is the most appropriate alternative to a CDK 4/6 inhibitor.
- Where the breast cancer has a PIK3CA mutation, NICE technology appraisal [816](#) recommends alpelisib plus fulvestrant for treating hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer when the condition has progressed after a CDK4/6 inhibitor plus an aromatase inhibitor.
- Where the breast cancer has a BRCA mutation, NICE technology appraisal [952](#) recommends talazoparib for treating HER2-negative, advanced breast cancer in people with hormone receptor-positive breast cancer after an anthracycline or a taxane, or both, and endocrine therapy unless it is not suitable.

For people who have decided to be treated with chemotherapy on progression to advanced disease, CG81 recommends offering systemic sequential therapy to most people:

- Where anthracyclines are not suitable (because they are contraindicated or because of prior anthracycline treatment) the sequencing should follow: single-agent docetaxel as a first-line treatment, single-agent vinorelbine or capecitabine as second-line treatment, and single-agent capecitabine or vinorelbine (whichever was not used as second-line treatment) as third-line treatment.
- NICE technology appraisal [116](#) recommends gemcitabine with paclitaxel for treating metastatic breast cancer only when docetaxel monotherapy or docetaxel plus capecitabine are also considered appropriate.
- NICE technology appraisal [423](#) recommends eribulin for treating locally advanced or metastatic breast cancer when it has progressed after at least 2 chemotherapy regimens.

The technology

Imlunestrant (brand name unknown, Eli Lilly and Company) does not currently have a marketing authorisation in the UK for oestrogen receptor-positive, HER2-negative advanced breast cancer after endocrine therapy. Imlunestrant with or without abemaciclib has been studied in a clinical trial compared with endocrine therapy for

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the treatment of locally advanced or metastatic oestrogen receptor-positive, HER2-negative breast cancer.

Intervention(s)	Imlunestrant with or without abemaciclib
Population(s)	People with oestrogen receptor-positive, HER2-negative locally advanced or metastatic breast cancer after endocrine treatment
Comparators	<p>After endocrine-based therapy:</p> <ul style="list-style-type: none"> • Everolimus and exemestane • CDK 4/6 inhibitors (abemaciclib, ribociclib or palbociclib) in combination with fulvestrant • Alpelisib plus fulvestrant, where the breast cancer has a PIK3CA mutation • Talazoparib, where the breast cancer has a BRCA mutation • Chemotherapy • Capivasertib [subject to a NICE evaluation] • Elacestrant, where the breast cancer has a ESR1 mutation [subject to a NICE evaluation]
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • progression-free survival • response rate • duration of response • adverse effects of treatment • health-related quality of life.

<p>Economic analysis</p>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.</p> <p>The availability and cost of biosimilar and generic products should be taken into account.</p>
<p>Other considerations</p>	<p>Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.</p>
<p>Related NICE recommendations</p>	<p>Related technology appraisals</p> <p>Talazoparib for treating HER2-negative advanced breast cancer with germline BRCA mutations (2024) NICE technology appraisal guidance 952.</p> <p>Palbociclib with fulvestrant for treating hormone receptor-positive, HER2-negative advanced breast cancer after endocrine therapy (2022) NICE technology appraisal guidance 836.</p> <p>Apelisisib with fulvestrant for treating hormone receptor-positive, HER2-negative, PIK3CA-mutated advanced breast cancer (2022) NICE technology appraisal guidance 816.</p> <p>Abemaciclib with fulvestrant for treating hormone receptor-positive, HER2-negative advanced breast cancer after endocrine therapy (2021) NICE technology appraisal guidance 725.</p> <p>Ribociclib with fulvestrant for treating hormone receptor-positive, HER2-negative advanced breast cancer after endocrine therapy (2021) NICE technology appraisal guidance 687.</p> <p>Abemaciclib with an aromatase inhibitor for previously untreated, hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer (2019) NICE technology appraisal guidance 563.</p> <p>Ribociclib with an aromatase inhibitor for previously untreated, hormone receptor-positive, HER2-negative, locally</p>

	<p>advanced or metastatic breast cancer (2017) NICE technology appraisal guidance 496.</p> <p>Palbociclib with an aromatase inhibitor for previously untreated, hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer (2017) NICE technology appraisal guidance 495.</p> <p>Eribulin for treating locally advanced or metastatic breast cancer after 2 or more chemotherapy regimens (2016) NICE technology appraisal guidance 423.</p> <p>Everolimus with exemestane for treating advanced breast cancer after endocrine therapy (2016) NICE technology appraisal 421.</p> <p>Fulvestrant for the treatment of locally advanced or metastatic breast cancer (2011) NICE technology appraisal guidance 239.</p> <p>Gemcitabine for the treatment of metastatic breast cancer (2007). NICE technology appraisal 116.</p> <p>Related technology appraisals in development:</p> <p>Capivasertib with fulvestrant for treating hormone receptor-positive HER2-negative advanced breast cancer after endocrine treatment [ID6370]. Publication date to be confirmed</p> <p>Vepdegestrant for treating hormone receptor-positive HER2-negative metastatic breast cancer after endocrine treatment [ID6360]. Publication date to be confirmed</p> <p>Datopotamab deruxtecan for previously treated hormone receptor-positive HER2-negative unresectable or metastatic breast cancer [ID6348]. Publication date to be confirmed</p> <p>Pembrolizumab with chemotherapy for treating hormone receptor-positive HER2-negative locally recurrent inoperable or metastatic breast cancer [ID6285]. Publication date to be confirmed</p> <p>Elacestrant for treating oestrogen receptor-positive, HER2-negative advanced breast cancer with an ESR1 mutation after at least 1 endocrine therapy [ID6225] Publication date to be confirmed</p> <p>Sacituzumab govitecan for treating hormone receptor-positive HER2-negative metastatic breast cancer after 2 or more therapies [ID4033] Publication date to be confirmed</p> <p>Taselisib for previously treated ER-positive, HER2-negative, PIK3CA-positive breast cancer in postmenopausal women [ID1401] Publication date to be confirmed</p> <p>Related NICE guidelines:</p> <p>Advanced breast cancer diagnosis and treatment (2009; updated 2017) NICE guideline CG81</p>
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	<p>Early and locally advanced breast cancer: diagnosis and management (2018; updated 2024) NICE guideline NG101</p> <p>Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer (2013; updated 2019) NICE guidance CG164</p> <p>Improving outcomes in breast cancer (2002; reviewed 2014) NICE guideline CSG1</p> <p>MammaTyper in vitro diagnostic test for determining breast cancer subtypes (2018) NICE Medtech Innovation Briefing 135</p> <p>Related quality standards:</p> <p>Breast cancer (2011; updated 2016) NICE quality standard 12.</p>
<p>Related National Policy</p>	<p>The NHS Long Term Plan (2019) NHS Long Term Plan</p> <p>NHS England (2023) Manual for prescribed specialist services (2023/2024) Chapter 105</p>

Questions for consultation

Where do you consider imlunestrant will fit into the existing care pathway for oestrogen receptor-positive, HER2-negative advanced breast cancer?

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 be expected to receive imlunestrant as monotherapy or in combination with abemaciclib?

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 oestrogen receptor-positive, HER2-negative advanced breast cancer 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?

Have all relevant comparators for imlunestrant with or without abemaciclib been included in the scope?

Would imlunestrant with or without abemaciclib be a candidate for managed access?

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.

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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at <https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation>).

References

1. NHS Digital (2023) [Cancer registration statistics, England, 2021- First release, counts only](#). Accessed April 2024.
2. Cancer Research UK (2022) [Early diagnosis data hub](#). Accessed April 2024.
3. Dewis R and Gribbin J (2009) [Breast cancer: diagnosis and treatment, an assessment of need](#). Cardiff: National Collaborating Centre for Cancer. Accessed April 2024.
4. Jin X, Zhou YF, Ma D, et al. (2023) [Molecular classification of hormone receptor-positive HER2-negative breast cancer](#). Nature Genetics 55:1696-1708.
5. Brett JO, Spring LM, Bardia A. et al. (2021) [ESR1 mutation as an emerging clinical biomarker in metastatic hormone receptor-positive breast cancer](#). Breast Cancer Research 23:85.