NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

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

Final scope

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 2022 in England, 50,978 people were diagnosed with breast cancer.[1] Approximately 12% of people with breast cancer in England in 2022 had advanced stage disease (stage 3 or 4) when they were diagnosed.[1,2] The 1-year survival rate for adults diagnosed at stage 4 (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, which may include surgery for early and locally advanced disease. 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.

- Endocrine therapy is the first-line treatment for most people with oestrogen receptor-positive advanced breast cancer. The choice of endocrine therapy is guided by NICE clinical guideline 81 (CG81). In people who have been through the menopause, endocrine therapies include steroidal or non-steroidal aromatase inhibitors. People who are before menopause or around menopause will have first-line treatment with tamoxifen and ovarian suppression, or ovarian suppression alone if they have previously had tamoxifen and then had disease progression. Men may have tamoxifen as a first-line endocrine treatment.
- 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.

- 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 ribociclib, abemaciclib 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.
- If 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.
- If the breast cancer has 1 or more PIK3CA, AKT1 or PTEN gene alterations, NICE technology appraisal 1063 recommends capivasertib with fulvestrant after a CDK4/6 inhibitor plus an aromatase inhibitor.
- If the breast cancer has an activating ESR1 mutation, NICE technology appraisal 1036 recommends elacestrant after at least 1 line of endocrine treatment plus a CDK4/6 inhibitor.
- If the breast cancer has a BRCA mutation, NICE technology appraisals 952 and 1040 recommend talazoparib or olaparib, respectively, 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.
- If 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 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
Subgroup(s)	If the evidence allows the following subgroups will be considered: • breast cancer with and without an ESR1 mutation • line of treatment.
Comparators	• Everolimus with exemestane • CDK 4/6 inhibitor (abemaciclib, ribociclib or palbociclib) with fulvestrant • Alpelisib with fulvestrant, if the breast cancer has a PIK3CA mutation • Talazoparib or olaparib, if the breast cancer has a BRCA mutation • Chemotherapy • Capivasertib with fulvestrant, if the breast cancer has 1 or more PIK3CA, AKT1 or PTEN gene alterations • Elacestrant, if the breast cancer has a ESR1 mutation
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • duration of response • adverse effects of treatment • health-related quality of life.

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. 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. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability and cost of biosimilar and generic products should be taken into account. The economic modelling should include the costs associated with diagnostic testing for the ESR1 mutation in people with oestrogen receptor-positive, HER2-negative locally advanced or metastatic breast cancer who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).
Other considerations	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.
Related NICE recommendations	**Related technology appraisals** Capivasertib with fulvestrant for treating hormone receptor-positive HER2-negative advanced breast cancer after endocrine treatment (2025) NICE technology appraisal guidance 1063 Olaparib for treating BRCA mutation-positive HER2-negative advanced breast cancer after chemotherapy (2025) NICE technology appraisal guidance 1040 Elacestrant for treating oestrogen receptor-positive, HER2-negative advanced breast cancer with an ESR1 mutation after at least 1 endocrine therapy (2025). NICE technology appraisal guidance 1036 Talazoparib for treating HER2-negative advanced breast cancer with germline BRCA mutations (2024) NICE technology appraisal guidance 952

	Palbociclib with fulvestrant for treating hormone receptor-positive, HER2-negative advanced breast cancer after endocrine therapy (2022) NICE technology appraisal guidance 836 Alpelisib with fulvestrant for treating hormone receptor-positive, HER2-negative, PIK3CA-mutated advanced breast cancer (2022) NICE technology appraisal guidance 816 Abemaciclib with fulvestrant for treating hormone receptor-positive, HER2-negative advanced breast cancer after endocrine therapy (2021) NICE technology appraisal guidance 725 Ribociclib with fulvestrant for treating hormone receptor-positive, HER2-negative advanced breast cancer after endocrine therapy (2021) NICE technology appraisal guidance 687 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 Ribociclib with an aromatase inhibitor for previously untreated, hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer (2017) NICE technology appraisal guidance 496 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 Eribulin for treating locally advanced or metastatic breast cancer after 2 or more chemotherapy regimens (2016) NICE technology appraisal guidance 423 Everolimus with exemestane for treating advanced breast cancer after endocrine therapy (2016) NICE technology appraisal 421 Fulvestrant for the treatment of locally advanced or metastatic breast cancer (2011) NICE technology appraisal guidance 239 Gemcitabine for the treatment of metastatic breast cancer (2007). NICE technology appraisal 116 **Related technology appraisals in development:** Inavolisib with palbociclib and fulvestrant for treating recurrent hormone receptor-positive HER2-negative PIK3CA-positive advanced breast cancer after adjuvant endocrine treatment [ID6425]. Publication date to be confirmed Vepdegestrant for treating hormone receptor-positive HER2-negative metastatic breast cancer after endocrine treatment [ID6360]. Publication date to be confirmed

	Datopotamab deruxtecan for previously treated hormone receptor-positive HER2-negative unresectable or metastatic breast cancer [ID6348]. Publication date to be confirmed Pembrolizumab with chemotherapy for treating hormone receptor-positive HER2-negative locally recurrent inoperable or metastatic breast cancer [ID6285]. Publication date to be confirmed Taselisib for previously treated ER-positive, HER2-negative, PIK3CA-positive breast cancer in postmenopausal women [ID1401] Publication date to be confirmed **Related NICE guidelines:** Advanced breast cancer diagnosis and treatment (2009; updated 2017) NICE guideline CG81 Early and locally advanced breast cancer: diagnosis and management (2018; updated 2025) NICE guideline NG101 Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer (2013; updated 2023) NICE guidance CG164 Improving outcomes in breast cancer (2002; reviewed 2014) NICE guideline CSG1 **Related NICE advice:** MammaTyper in vitro diagnostic test for determining breast cancer subtypes (2018) NICE Medtech innovation briefing 135 **Related quality standards:** Breast cancer (2011; updated 2016) NICE quality standard 12

References

1. NHS Digital (2024) Cancer registration statistics, England, 2022. Accessed August 2025.

2. Cancer Research UK (2022) Early diagnosis data hub. Accessed August 2025.

3. Dewis R and Gribbin J (2009) Breast cancer: diagnosis and treatment, an assessment of need. Cardiff: National Collaborating Centre for Cancer. Accessed August 2025.

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.