

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Elacestrant for treating oestrogen receptor-positive HER2-negative advanced breast cancer with an ESR1 mutation after at least 1 endocrine treatment [ID6225]

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of elacestrant within its marketing authorisation for treating oestrogen receptor-positive, HER2-negative locally advanced or metastatic breast cancer with an activating ESR1 mutation that has progressed after at least 1 line of endocrine therapy including a CDK 4/6 inhibitor in people who have been through the menopause and men.

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 2020 in England, 40,192 people were diagnosed with breast cancer.¹ Approximately 14.8% of people with breast cancer in England in 2020 had advanced stage disease (stage III or IV) when they were diagnosed.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 1 (ESR1) mutations are found in 20% to 40% of people with metastatic breast cancer after aromatase inhibition.⁵

NICE technology appraisals [495](#), [496](#) and [563](#) recommend cyclin-dependent kinase 4 and 6 (CDK 4/6) inhibitors (palbociclib, ribociclib and abemaciclib respectively) in a combination with an aromatase inhibitor for treating hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer as an initial endocrine-based therapy in adults. [NICE clinical guideline 81](#) (CG81) recommends first-line treatment with endocrine therapy for most people with advanced hormone receptor-positive breast cancer. But for people whose disease is life-threatening or requires early relief of symptoms, CG81 recommends chemotherapy, followed by endocrine therapy. The endocrine therapies used in clinical practice in people who have been through the menopause include non-steroidal aromatase inhibitors (anastrozole and letrozole) or tamoxifen, if aromatase inhibitors are not tolerated or are contraindicated. Men may receive tamoxifen as a first-line endocrine treatment.

Final scope for the evaluation of elacestrant for treating oestrogen receptor-positive HER2-negative advanced breast cancer with an ESR1 mutation after at least 1 endocrine treatment [ID6225]

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For people who have been through the menopause and 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. NICE technology appraisal [816](#) recommends alpelisib plus fulvestrant for treating hormone receptor-positive, HER2-negative, PIK3CA-mutated, locally advanced or metastatic breast cancer when the condition has progressed after a CDK4/6 inhibitor plus an aromatase inhibitor.

CG81 recommends systemic sequential therapy for most people with advanced breast cancer having chemotherapy. 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

Elacestrant (Korserdu, Menarini Stemline) has a marketing authorisation in the UK for the treatment of people who have been through the menopause, and men, with oestrogen receptor-positive, HER2-negative, locally advanced or metastatic breast cancer with an activating ESR1 mutation who have disease progression following at least 1 line of endocrine therapy including a CDK 4/6 inhibitor.

Intervention(s)	Elacestrant
Population(s)	People who have been through the menopause and men with oestrogen receptor-positive HER2-negative locally advanced or metastatic breast cancer with an activating ESR1 mutation after at least 1 line of endocrine therapy including a CDK 4/6 inhibitor
Subgroups	If the evidence allows the following subgroups will be considered: <ul style="list-style-type: none"> • Mutations in both ESR1 and PIK3CA

Comparators	<ul style="list-style-type: none"> • Everolimus and exemestane • Endocrine therapy with or without chemotherapy • Chemotherapy <p>For people whose breast cancer is PIK3CA-mutated:</p> <ul style="list-style-type: none"> • Alpelisib plus fulvestrant
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • progression-free survival • response rate • adverse effects of treatment • health-related quality of life.
Economic analysis	<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>The economic modelling should include the costs associated with diagnostic testing for ESR1 and where relevant, PIK3CA mutations 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).</p>
Other considerations	<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>Palbociclib with fulvestrant for treating hormone receptor-positive, HER2-negative advanced breast cancer after endocrine therapy (2022) NICE technology appraisal guidance 836.</p> <p>Alpelisib 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 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>Gemcitabine for the treatment of metastatic breast cancer (2007). NICE technology appraisal 116.</p> <p>Related technology appraisals in development</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>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; checked 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>
Related National Policy	<p>The NHS Long Term Plan (2019) NHS Long Term Plan</p> <p>NHS England (2023) NHS manual for prescribed specialist services (2023/2024) Chapter 105.</p>

References

1. NHS Digital (2022) [Cancer registration statistics, England, 2020](#). Accessed February 2024.
2. Cancer Research UK (2022) [Early diagnosis data hub](#). Accessed February 2024.
3. Dewis R and Gribbin J (2009) [Breast cancer: diagnosis and treatment, an assessment of need](#). Cardiff: National Collaborating Centre for Cancer. Accessed February 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.