NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Elacestrant for treating postmenopausal hormone receptor-positive HER2-negative advanced or metastatic breast cancer after 1 or 2 endocrine treatments

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of elacestrant within its marketing authorisation for treating postmenopausal hormone receptor-positive HER2-negative advanced or metastatic breast cancer after 1 or 2 endocrine treatments.

Background

Breast cancer arises from the tissues of the ducts or lobules of the breast. The cancer is said to be metastatic if it has spread to other parts of the body such as the bones, liver, and lungs.

In 2020 in England, 40,192 people were diagnosed with breast cancer.[1] Approximately 5.6% of people with breast cancer in England in 2020 had stage IV (metastatic) breast cancer when they were diagnosed.[2] The 1-year survival rate for adults diagnosed at stage IV 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. Approximately 56% of women with advanced (metastatic) breast cancer in the UK have hormone receptor-positive, human epidermal growth factor receptor 2 (HER2)-negative disease.[4]

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. The endocrine therapies used in clinical practice in postmenopausal people include aromatase inhibitors (anastrozole and letrozole) or tamoxifen, if aromatase inhibitors are not tolerated or are contraindicated. Women who are premenopausal or perimenopausal will receive first-line treatment with tamoxifen and ovarian suppression if they have not previously received tamoxifen, while men will receive tamoxifen as a first-line endocrine treatment. 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 initial endocrine based therapy in adults. Fulvestrant is not recommended for untreated locally advanced or metastatic oestrogen-receptor positive breast cancer (NICE technology appraisal 503).

For people who receive first-line treatment with anastrozole or letrozole, second-line treatment may be either tamoxifen, exemestane, or everolimus and exemestane (NICE technology appraisal 421). Subsequent treatment options also include chemotherapy for some people. NICE technology appraisals 687, 725 and 836 recommend abemaciclib, ribociclib and palbociclib with fulvestrant for treating hormone receptor-positive, HER2-negative, advanced breast cancer in people who have had previous endocrine therapy (when exemestane plus everolimus is the most appropriate alternative to a CDK 4/6 inhibitor). Fulvestrant is not recommended for use following anti-oestrogen therapy, as an alternative to aromatase inhibitors (NICE technology appraisal 239), however, it is sometimes used after exemestane and tamoxifen in people who would otherwise receive chemotherapy. 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 cancer has progressed after a CDK4/6 inhibitor plus an aromatase inhibitor.

The technology

Elacestrant (Orserdu, Menarini Group) does not currently have a marketing authorisation in the UK for treating postmenopausal hormone receptor-positive HER2-negative advanced or metastatic breast cancer after 1 or 2 endocrine treatments. It is being studied in a phase 3 clinical trial compared with standard of care (fulvestrant, anastrozole, letrozole, or exemestane) in people with hormone receptor-positive HER2-negative advanced breast cancer after 1 or 2 prior lines of endocrine treatment, including 1 line containing a CDK4/6 inhibitor.

Intervention(s)	Elacestrant
Population(s)	Postmenopausal hormone receptor-positive HER2-negative advanced or metastatic breast cancer after 1 or 2 endocrine treatments
Subgroups	If the evidence allows the following subgroups will be considered: • Mutations in estrogen receptor 1 (ESR1)

Comparators	• Everolimus and exemestane • Exemestane • Tamoxifen • Fulvestrant • Paclitaxel • Capecitabine For people who haven't previously had a CDK 4/6 inhibitor in combination with AI: • CDK 4/6 inhibitors (abemacicilib, ribociclib or palbociclib) in combination with fulvestrant For people whose cancer is PIK3CA-mutated: • Alpelisib plus fulvestrant
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • 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.
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:**

	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 endocrine therapy for adjuvant treatment of hormone receptor-positive, HER2-negative, node-positive early breast cancer at high risk of recurrence (2022) NICE technology appraisal guidance 810. 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:**

	Ribociclib with endocrine therapy for adjuvant treatment of hormone receptor-positive, HER2-negative early breast cancer [ID6153] Publication date to be confirmed Sacituzumab govitecan for treating hormone receptor-positive HER2-negative metastatic breast cancer after 2 or more therapies [ID4033] Publication date to be confirmed Ribociclib in combination with endocrine therapy and goserelin for previously untreated hormone receptor-positive, HER2-negative advanced breast cancer in premenopausal women [ID1301] 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 2023) 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 2019) NICE guidance CG164 Improving outcomes in breast cancer (2002; checked 2014) NICE guideline CSG1 MammaTyper in vitro diagnostic test for determining breast cancer subtypes (2018) NICE Medtech Innovation Briefing 135 **Related NICE guidelines in development:** Early and locally advanced breast cancer: diagnosis and management - further surgery (update). NICE guideline. Publication date to be confirmed **Related quality standards:** Breast cancer (2011; updated 2016) NICE quality standard 12
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2018) NHS manual for prescribed specialist services (2018/2019)

Questions for consultation

Where do you consider elacestrant will fit into the existing care pathway for postmenopausal hormone receptor-positive HER2-negative advanced or metastatic breast cancer?

The phase 3 trial of elacestrant versus standard of care for the treatment of patients with ER+/HER2- advanced breast cancer has reported results in all patients and patients with detectable ESR1 mutations. Are ESR1 mutations routinely tested for in hormone receptor-positive HER2-negative advanced breast cancer in NHS practice?

Would elacestrant be a candidate for managed access?

Do you consider that the use of elacestrant 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 elacestrant 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 (2022) Cancer registration statistics, England, 2020. Accessed July 2023.
2. Cancer Research UK (2022) Early diagnosis data hub. Accessed July 2023.
3. Dewis R and Gribbin J (2009) Breast cancer: diagnosis and treatment, an assessment of need. Cardiff: National Collaborating Centre for Cancer. Accessed May 2022.
4. NICE (2017) Palbociclib with an aromatase inhibitor for previously untreated, hormone receptor positive, HER2-negative, locally advanced or metastatic breast cancer (TA495). Accessed May 2022.