NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Giredestrant with everolimus for treating oestrogen-receptor positive HER2-negative advanced breast cancer after cyclin-dependent kinase 4 and 6 inhibitor and endocrine treatment ID6576

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of giredestrant with everolimus within its marketing authorisation for treating oestrogen-receptor positive HER2-negative advanced breast cancer after a cyclin-dependent kinase 4 and 6 inhibitor and 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, 50,980 people were diagnosed with breast cancer.[1] Approximately 15% of people with breast cancer in England in 2022 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, 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.

- Endocrine therapy is the first-line treatment for most people with oestrogen receptor-positive advanced breast cancer. The choice of endocrine therapy for advanced breast cancer 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.

- For people whose disease is life-threatening or requires early relief of symptoms, CG81 recommends chemotherapy first, followed by endocrine therapy. For people who have decided to be treated with chemotherapy on

progression to advanced disease CG81 recommends offering systemic sequential therapy to most people.

For people whose hormone receptor-positive, HER2-negative advanced breast cancer has recurred or progressed after previous endocrine therapy:

- 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.

- NICE technology appraisals 952 and 1040 recommend talazoparib or olaparib, respectively, for treating hormone receptor-positive HER2-negative, advanced breast cancer with germline BRCA1 or BRCA2 mutations after an anthracycline or a taxane, or both, and endocrine therapy, unless it is not suitable

- NICE technology appraisal 1036 recommends elacestrant 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 treatment plus a CDK 4/6 inhibitor

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.

- Where the breast cancer has a PIK3CA mutation, NICE technology appraisal 816 recommends alpelisib plus fulvestrant and 1063 recommends capivasertib 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.

The technology

Giredestrant (brand name unknown, Roche) does not currently have a marketing authorisation in the UK for treating oestrogen-receptor positive HER2-negative advanced breast cancer after CDK 4/6 inhibitor and endocrine treatment. Giredestrant with everolimus has been studied in a clinical trial for treating oestrogen-receptor positive HER2-negative advanced breast cancer after CDK 4/6 inhibitor and endocrine treatment, compared with endocrine therapy plus everolimus.

Intervention(s)	Giredestrant with everolimus
Population(s)	People with oestrogen-receptor positive HER2-negative advanced breast cancer after CDK 4/6 inhibitor and endocrine treatment

Subgroups	If the evidence allows the following subgroups will be considered:
	• Breast cancer with and without a mutation in:
	  ○ ESR1
	  ○ PIK3CA
	  ○ AKT1
	  ○ PTEN
	  ○ BRCA
	• Line of therapy

Comparators	• Everolimus with exemestane • Alpelisib with fulvestrant, if the breast cancer has PIK3CA mutation • Talazoparib or olaparib, if the breast cancer has a BRCA mutation • Capivasertib with fulvestrant, if the breast cancer has 1 or more PIK3CA, AKT1 or PTEN gene alterations • Elacestrant, if the breast cancer has an ESR1 mutation • CDK 4/6 inhibitor (abemaciclib, ribociclib or palbociclib) with fulvestrant • Endocrine therapy (such as tamoxifen, letrozole or anastrazole) with or without chemotherapy • Chemotherapy • Inavolisib with palbociclib and fulvestrant (subject to NICE appraisal) • Imlunestrant with or without abemaciclib (subject to NICE appraisal) • Sacituzumab govitecan (subject to NICE appraisal) • Daptotamab deruxtecan (subject to NICE appraisal) • Pembrolizumab with chemotherapy (subject to NICE appraisal)

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.
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 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. Fulvestrant for untreated locally advanced or metastatic oestrogen-receptor positive breast cancer (2018) NICE technology appraisal guidance 503. 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. 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 [6425] Publication date to be confirmed

	Imlunestrant for treating oestrogen receptor-positive HER2-negative advanced breast cancer after endocrine therapy [ID6373] 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 Sacituzumab govitecan for treating hormone receptor-positive HER2-negative advanced breast cancer after endocrine treatment [ID6593] 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 2024) 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; 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 - Neoadjuvant chemotherapy and ovarian function suppression (update). Expected publication date 2025 **Related quality standards:** Breast cancer (2011; updated 2016) NICE quality standard 12

Questions for consultation

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

Have all relevant comparators for giredestrant with everolimus been included in the scope?

Are the suggested subgroups appropriate?

Please select from the following, will giredestrant with everolimus be:
A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):
For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Would giredestrant with everolimus be a candidate for managed access?

Do you consider that the use of giredestrant with everolimus 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 giredestrant with everolimus 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 (2024) Cancer registration statistics, England, 2022. Accessed October 2025.

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

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