NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Inavolisib with palbociclib and fulvestrant for treating recurrent hormone receptor-positive HER2-negative PIK3CA-positive advanced breast cancer after adjuvant endocrine treatment ID6425

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of inavolisib with palbociclib and fulvestrant within its marketing authorisation for treating recurrent hormone receptor-positive HER2-negative, PIK3CA-positive advanced breast cancer after adjuvant 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] PIK3CA gene mutations are found in 30% to 40% of oestrogen receptor positive, HER2-negative tumours.[5]

NICE technology appraisals 495, 496 and 563 recommend use of an aromatase inhibitor (a type of endocrine therapy) 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 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 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.

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

Inavolisib (brand name unknown, Roche) does not currently have a marketing authorisation in the UK for hormone receptor-positive HER2-negative, PIK3CA-positive advanced breast cancer after endocrine therapy. Inavolisib plus palbociclib and fulvestrant has been studied in a clinical trial compared with placebo plus palbociclib and fulvestrant for the treatment of hormone receptor-positive HER2-

negative, PIK3CA-positive locally advanced or metastatic breast cancer that has progressed during or after adjuvant endocrine treatment.

Intervention(s)	Inavolisib with palbociclib and fulvestrant
Population(s)	People with recurrent hormone receptor-positive HER2-negative, PIK3CA-positive advanced breast cancer after adjuvant endocrine treatment
Comparators	After endocrine-based therapy: • 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 • Capivasertib with fulvestrant [subject to a NICE evaluation] • Elacestrant, where the breast cancer has a ESR1 mutation [subject to a NICE evaluation] • Imlunestrant with or without abemaciclib [subject to a NICE evaluation]
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.

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 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: Imlunestrant for treating oestrogen receptor-positive HER2-negative advanced breast cancer after endocrine therapy [ID6373]. Publication date to be confirmed Capivasertib with fulvestrant for treating hormone receptor-positive HER2-negative advanced breast cancer after endocrine treatment [ID6370]. Publication expected March 2025 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 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. Sacituzumab govitecan for treating hormone receptor-positive HER2-negative metastatic breast cancer after 2 or more therapies [ID4033] 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 2019) NICE guidance CG164 Improving outcomes in breast cancer (2002; reviewed 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: Advanced breast cancer: diagnosis and treatment (Partial update) NICE guideline. Publication date to be confirmed Breast cancer guidelines. NICE guideline. Publication date to be confirmed Early and locally advanced breast cancer: diagnosis and management - Neoadjuvant chemotherapy and ovarian function suppression (update). NICE guideline. Publication expected March 2025 Lymphoedema: prevention and management in people with early, locally advanced, and advanced breast cancer (update). NICE guideline. Publication date to be confirmed **Related quality standards:** Breast cancer (2011; updated 2016) NICE quality standard 12.

Questions for consultation

Where do you consider inavolisib with palbociclib and fulvestrant will fit into the existing care pathway for recurrent hormone receptor-positive HER2-negative, PIK3CA-positive advanced breast cancer after adjuvant endocrine treatment?

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

Are there any subgroups of people in whom inavolisib with palbociclib and fulvestrant is expected to be more clinically effective and cost effective?

Have all relevant comparators for inavolisib with palbociclib and fulvestrant been included in the scope?

Would inavolisib with palbociclib and fulvestrant be a candidate for managed access?

Do you consider that the use of inavolisib with palbociclib and fulvestrant 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.

Please indicate if any of the treatments in the scope are used in NHS practice differently than advised in their Summary of Product Characteristics. For example, if the dose or dosing schedule for a treatment is different in clinical practice. If so, please indicate the reasons for different usage of the treatment(s) in NHS practice. If stakeholders consider this a relevant issue, please provide references for data on the efficacy of any treatments in the pathway used differently than advised in the Summary of Product Characteristics.

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 inavolisib with palbociclib and fulvestrant 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 November 2024.

2. Cancer Research UK (2022) Early diagnosis data hub. Accessed November 2024.

3. Dewis R and Gribbin J (2009) Breast cancer: diagnosis and treatment, an assessment of need. Cardiff: National Collaborating Centre for Cancer. Accessed November 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. Kratz J, Burkard M, O'Meara T, et al (2018) Incorporating Genomics Into the Care of Patients With Advanced Breast Cancer. American Society of Clinical Oncology. Volume 38, 56-64. Accessed November 2024.