NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Capivasertib with fulvestrant for treating hormone receptor-positive HER2-negative advanced breast cancer after endocrine treatment ID6370

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of capivasertib with fulvestrant within its marketing authorisation for treating hormone receptor-positive, HER2-negative locally advanced or metastatic 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 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]

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. 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. 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 who have been through menopause and whose hormone receptor-positive, HER2-negative advanced breast cancer has recurred or progressed after a non-steroidal aromatase inhibitor, second-line treatment may be either tamoxifen,

exemestane, or everolimus and exemestane (NICE technology appraisal 421). 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 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.

The technology

Capivasertib (Truqap, AstraZeneca UK Ltd) with fulvestrant does not currently have a marketing authorisation in the UK for hormone receptor-positive HER2-negative advanced breast cancer following recurrence or progression on or after an endocrine based regimen. It has been studied in a clinical trial compared with placebo with fulvestrant in adults with locally advanced or metastatic hormone receptor-positive, HER2-negative breast cancer following recurrence or progression on or after aromatase inhibitor therapy.

Intervention(s)	Capivasertib with fulvestrant
Population(s)	Adults with hormone receptor-positive, HER2-negative locally advanced or metastatic breast cancer after endocrine treatment
Subgroups	If the evidence allows the following subgroups should be considered: • PIK3CA/AKT1/PTEN-altered subgroup

Comparators	• CDK4/6 inhibitors in combination with fulvestrant
	  ○ Abemaciclib
	  ○ Ribociclib
	  ○ Palbociclib
	• Everolimus and exemestane
	• Exemestane
	• Tamoxifen
	• Endocrine therapy with or without chemotherapy
	• Chemotherapy
	For people whose breast 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. The availability and cost of biosimilar and generic products should be taken into account. The economic modelling should include the costs associated with PIK3CA/AKT1/PTEN mutations in people with hormone 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:** 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. 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: 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 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 Taselisib for previously treated ER-positive, HER2-negative, PIK3CA-positive breast cancer in postmenopausal women [ID1401] 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 [ID1307] 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). 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 (2023) NHS manual for prescribed specialist services (2023)

Questions for consultation

Where do you consider capivasertib with fulvestrant will fit into the existing care pathway for hormone receptor-positive HER2-negative advanced breast cancer?

Have all relevant comparators for capivasertib with fulvestrant been included in the scope? In particular, are exemestane and tamoxifen appropriate comparators?

Would capivasertib with fulvestrant be a candidate for managed access?

Do you consider that the use of capivasertib with 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.

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 capivasertib with 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 (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. NICE (2017) Palbociclib with an aromatase inhibitor for previously untreated, hormone receptor positive, HER2-negative, locally advanced or metastatic breast cancer (TA495).