NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Palbociclib in combination with fulvestrant for treating advanced, hormone-receptor positive, HER2-negative breast cancer after endocrine therapy (review TA619)

Draft scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of palbociclib within its marketing authorisation for treating advanced hormone receptor-positive, HER2-negative breast cancer.

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 2017 in England, around 46,109 people were diagnosed with breast cancer.[1] In 2018 there were 9,640 deaths from breast cancer in England.[2] The 1-year survival rate for adults diagnosed at stage IV (metastatic breast cancer) in England is 66%. [3] Approximately 13% of women with breast cancer have advanced disease when they are diagnosed,[4] and around 35% of people with early or locally advanced disease will progress to metastatic breast cancer in the 10 years following diagnosis.[5] Most (80%) breast cancers are hormone-receptor positive and around two-thirds are oestrogen receptor positive. Human epidermal growth factor receptor 2 (HER2) is present in about 15-25% of breast cancers.[6] Approximately 64% of women with metastatic breast cancer in the UK have hormone-receptor positive, HER2 negative disease.[7]

Current treatments for advanced breast cancer aim to relieve symptoms, prolong survival and maintain a good quality of life with few adverse events. Treatment depends on whether the cancer cells have particular receptors (hormone receptor status or human epidermal growth factor receptor 2 [HER2] status), the extent of the disease and previous treatments.

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 and 496 recommend palbociclib with an aromatase inhibitor and ribociclib with and 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 and 725 recommend abemaciclib and ribociclib 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). NICE technology appraisal 619 recommends palbociclib in the same population for use within the Cancer Drugs Fund. This appraisal will update and replace technology appraisal 619. 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.

The technology

Palbociclib (Ibrance, Pfizer) is a selective, small-molecule inhibitor of cyclin-dependent kinases 4 and 6, which prevents DNA synthesis by prohibiting progression of the cell cycle from G1 to S phase. Palbociclib is administered orally.

Palbociclib has a marketing authorisation in the UK for the treatment of hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative locally advanced or metastatic breast cancer: in combination with an aromatase inhibitor; in combination with fulvestrant in women who have received prior endocrine therapy. In pre- or perimenopausal women, the endocrine therapy should be combined with a luteinizing hormone releasing hormone (LHRH) agonist.

Intervention(s)	Palbociclib in combination with fulvestrant
Population(s)	People with hormone receptor-positive, HER2-negative locally advanced or metastatic breast cancer who have received prior endocrine therapy.

Comparators	• CDK4/6 inhibitors in combination with fulvestrant
	  ○ Abemaciclib
	  ○ Ribociclib
	• Everolimus and exemestane

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 patient access schemes for the comparator 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 and NICE	Related technology appraisals: Everolimus with exemestane for treating advanced breast cancer after endocrine therapy (2016) NICE technology appraisal

Pathways	421. Next review December 2019. Fulvestrant for the treatment of locally advanced or metastatic breast cancer (2011) NICE technology appraisal guidance 239. Review date Nov 2014. Review decision, static list Gemcitabine for the treatment of metastatic breast cancer (2007). NICE technology appraisal 116. Review date, May 2010. Review decision, static list. Alpelisib in combination with fulvestrant for treating advanced hormone-receptor positive, HER2-negative, PIK3CA-positive breast cancer (2020) NICE technology appraisal 652 (terminated appraisal). Abemaciclib with fulvestrant for treating advanced hormone-receptor positive, HER2-negative breast cancer after endocrine therapy (2021) NICE technology appraisal 725. Review date 2024. Ribociclib in combination with fulvestrant for treating advanced hormone-receptor positive, HER2-negative breast cancer (2021) NICE technology appraisal 687. Review date 2024 Appraisals in development: Alpelisib in combination with fulvestrant for treating advanced hormone-receptor positive, HER2-negative, PIK3CA-positive breast cancer. ID3929. Earliest publication July 2022. Related guidelines: Advanced breast cancer: diagnosis and treatment (2009, updated 2017). NICE guideline CG81. Review date 2017. Surveillance check in January 2018. Familial breast cancer: Classification and care of people at risk of familial breast cancer and management of breast cancer and related risks in people with a family history of breast cancer (2013, updated 2017). NICE guideline 164.Surveillance check in November 2019. Related quality standards: Breast cancer (2011, updated 2016). NICE quality standard 12. Related NICE Pathways: Advanced breast cancer (2020) NICE Pathway

	Familial breast cancer (2020) NICE Pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018) Manual for Prescribed Specialised Services 2018/19. Chapter 105, Specialist Cancer services (adults) Department of Health (2016) NHS Outcomes Framework 2016-2017. Domains 1 and 2.

Questions for consultation

Have all relevant comparators for palbociclib in combination with fulvestrant been included in the scope? Which treatments are considered to be established clinical practice in the NHS for hormone receptor-positive, HER2-negative locally advanced or metastatic breast cancer who have received prior endocrine therapy? Would fulvestrant, tamoxifen or exemestane monotherapy be considered appropriate comparators?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom palbociclib in combination with fulvestrant is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider palbociclib in combination with fulvestrant will fit into the existing NICE pathway, Advanced breast cancer ?

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 palbociclib in combination with fulvestrant is 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.

Do you consider palbociclib in combination with fulvestrant to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of palbociclib in combination with fulvestrant can result in any potential significant and 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 Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?
- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?
- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?
- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. Office for National Statistics (2019) Cancer registration statistics, England, 2017. Accessed January 2020.
2. Nomis (2020) Office for National Statistics. Mortality statistics – underlying cause, sex and age: 2018 data. Accessed January 2020.

3. Cancer Research UK (2020) Breast cancer incidence statistics: England 2014 data. Accessed January 2020

4. Cancer Research UK (2014) Breast cancer survival statistics. Accessed August 2017.

5. Dewis R and Gribbin J (2009) Breast cancer: diagnosis and treatment, an assessment of need. Cardiff: National Collaborating Centre for Cancer. Accessed August 2017.

6. NIHR Evidence Briefing. (2017) Alpelisib in combination with fulvestrant for advanced HR positive, HER2-negative breast cancer in men and postmenopausal women. Accessed September 2018.

7. NICE. (2017) Resource impact report: Palbociclib with an aromatase inhibitor for previously untreated, hormone receptor positive, HER2-negative, locally advanced or metastatic breast cancer (TA495). Accessed September 2018.