

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Proposed Health Technology Appraisal**

**Palbociclib for treating metastatic, hormone receptor-positive, HER2-negative breast cancer**

**Draft scope (pre-referral)**

**Draft remit/appraisal objective**

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

**Background**

Breast cancer arises from the tissues of the ducts or lobules of the breast. Metastatic breast cancer describes disease that has spread to another part of the body, such as the bones, liver, or lungs.

Over 44,800 people were diagnosed with breast cancer in England in 2013, and there were approximately 9800 deaths from breast cancer in 2012<sup>1,2</sup>. The 5-year survival rate for people with metastatic breast cancer in England is 15%<sup>3</sup>. Approximately 17% of women with invasive breast cancers have locally advanced or metastatic disease when they are diagnosed<sup>4</sup>, and around 35% of people with early or locally advanced disease will progress to metastatic breast cancer<sup>5,6</sup>.

Current treatments for metastatic breast cancer aim to relieve symptoms, prolong survival and maintain a good quality of life with few adverse events. Treatment may depend on whether the cancer cells have particular receptors (hormone receptor status or HER2 status), the extent of the disease and previous treatments. NICE Clinical Guideline 81 recommends that endocrine therapy should be offered as first-line treatment for the majority of people with hormone receptor-positive metastatic breast cancer. In clinical practice, people who are post-menopausal with hormone receptor-positive metastatic breast cancer often receive first-line treatment with anastrozole or letrozole. People who are pre- or peri-menopausal will receive first-line treatment with tamoxifen and ovarian suppression if they have not previously received tamoxifen. Chemotherapy should be offered as first-line treatment for people with hormone-receptor positive advanced breast cancer whose disease is imminently life-threatening or requires early relief of symptoms because of significant visceral organ involvement, providing they understand and are prepared to accept the toxicity.

For people who receive first-line treatment with anastrozole or letrozole, second-line treatment may be either tamoxifen or exemestane, followed by third-line treatment with exemestane or tamoxifen depending on the previous treatment received. 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. Subsequent treatment options also include anthracycline-based chemotherapy, taxane monotherapy (docetaxel, paclitaxel or nab-paclitaxel), single agent capecitabine, vinorelbine oral or intravenous preparations, gemcitabine monotherapy or gemcitabine with paclitaxel or carboplatin. Everolimus in combination with exemestane is currently available on the Cancer Drugs Fund for people with hormone receptor positive, HER2-negative breast cancer who have not had previous treatment with exemestane. NICE recommends gemcitabine in combination with paclitaxel as an option for the treatment of metastatic breast cancer only when docetaxel monotherapy or docetaxel plus capecitabine are also considered appropriate (technology appraisal no. 116).

### 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 taken orally.

Palbociclib does not currently have a marketing authorisation in the UK. It has been studied in a clinical trial in combination with fulvestrant compared with placebo and fulvestrant in people with metastatic hormone receptor-positive, HER2-negative breast cancer that has relapsed or progressed during prior endocrine therapy. Palbociclib has also been studied in a clinical trial in combination with letrozole compared with placebo and letrozole in post-menopausal women with previously untreated metastatic hormone receptor-positive, HER2-negative breast cancer.

<b>Intervention(s)</b>	Palbociclib in combination with endocrine therapy
<b>Population(s)</b>	<ul style="list-style-type: none"> <li>• Post-menopausal people with previously untreated, metastatic, hormone receptor-positive, HER2-negative breast cancer</li> <li>• People with metastatic, hormone receptor-positive, HER2-negative breast cancer that has progressed after endocrine therapy</li> </ul>

<p><b>Comparators</b></p>	<p>For postmenopausal people with untreated metastatic, hormone receptor-positive, HER2-negative breast cancer:</p> <ul style="list-style-type: none"> <li>• Aromatase inhibitors (such as letrozole or anastrozole)</li> <li>• Chemotherapy (in accordance with NICE guidance)</li> </ul> <p>For people with metastatic, hormone receptor-positive, HER2-negative breast cancer that has progressed after endocrine therapy:</p> <ul style="list-style-type: none"> <li>• Exemestane</li> <li>• Everolimus and exemestane (not recommended by NICE, available through the CDF)</li> <li>• Tamoxifen</li> <li>• Fulvestrant</li> <li>• Chemotherapy (in accordance with NICE guidance)</li> </ul>
<p><b>Outcomes</b></p>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• overall survival</li> <li>• progression free survival</li> <li>• response rate</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul>
<p><b>Economic analysis</b></p>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p>

<p><b>Other considerations</b></p>	<p>Guidance will only be issued in accordance with the marketing authorisation.</p> <p>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.</p>
<p><b>Related NICE recommendations and NICE Pathways</b></p>	<p>Related Technology Appraisals:</p> <p><a href="#">Everolimus in combination with exemestane for treating advanced HER2-negative hormone-receptor-positive breast cancer after endocrine therapy</a> (2013) NICE Technology Appraisal guidance 295. Review date June 2016.</p> <p><a href="#">‘Bevacizumab in combination with capecitabine for the first-line treatment of metastatic breast cancer’</a> (2012). NICE Technology Appraisal guidance 263. Review date June 2015. Next review date TBC</p> <p><a href="#">‘Bevacizumab in combination with a taxane for the first-line treatment of metastatic breast cancer’</a> (2011). NICE Technology Appraisal 214.</p> <p><a href="#">‘Fulvestrant for the treatment of locally advanced or metastatic breast cancer’</a> (2011). NICE Technology Appraisal 239. Review date Nov 2014. Review decision, static list</p> <p><a href="#">‘Gemcitabine for the treatment of metastatic breast cancer’</a> (2007). NICE technology Appraisal 116. Review date, May 2010. Review decision, static list.</p> <p>Appraisals in development (including suspended appraisals):</p> <p><a href="#">‘Sunitinib in combination with capecitabine within its licensed indication for the treatment of advanced and/or metastatic breast cancer’</a>. NICE Technology Appraisal guidance [ID319]. Suspended.</p> <p><a href="#">‘Sunitinib in combination with a taxane within its licensed indication for the first line treatment of advanced and/or metastatic breast cancer’</a>. NICE Technology Appraisal guidance [ID58]. Suspended.</p> <p>Related Guidelines:</p> <p><a href="#">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</a></p>

	<p><a href="#">history of breast cancer</a> (2013). NICE guideline CG164 Review date: December 2015</p> <p><a href="#">‘Advanced breast cancer: diagnosis and treatment’</a> (2009). NICE guideline 81 This guidance replaces previous Technology Appraisals No. 30, 54 and 62. Review date December 2015.</p> <p><a href="#">‘Breast cancer (early and locally advanced): diagnosis and treatment’</a> (2009). Clinical Guideline No. 80. Review decision date December 2015.</p> <p>Related Quality Standards:</p> <p><a href="#">‘Breast cancer’</a> (2011) NICE quality standard 12 (update expected June 2016).</p> <p><a href="http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp">http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp</a></p> <p>‘Related NICE Pathways:</p> <p><a href="#">Advanced breast cancer</a> (2015) NICE pathway</p> <p><a href="#">Familial breast cancer</a> (2015) NICE pathway</p> <p><a href="#">Early and locally advanced breast cancer</a> (2014) NICE pathway</p> <p><a href="http://pathways.nice.org.uk/">http://pathways.nice.org.uk/</a></p>
<p><b>Related National Policy</b></p>	<p>Chapter 105. Specialist Cancer services (adults)</p> <p><a href="http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf">http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf</a></p> <p>Department of Health, NHS Outcomes Framework 2014-2015, Nov 2013. Domain 1</p> <p><a href="https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf">https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf</a></p>

**Questions for consultation**

Which treatments are considered to be established clinical practice in the NHS for metastatic hormone receptor-positive, HER2-negative breast cancer?

- Are the comparators appropriate?
- Should chemotherapy be included as a comparator?
- Are there other relevant comparators for palbociclib?

Are the outcomes listed appropriate?

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

Where do you consider palbociclib will fit into the existing NICE pathways ([Early and locally advanced breast cancer](#) [2014] and [Advanced breast cancer](#) [2015])?

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 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.

Do you consider palbociclib 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 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.

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>)

### References

1. Office for National Statistics (2015) [Cancer registration statistics, England, 2013](#). Accessed September 2015.

2. Cancer Research UK (2014) [Breast cancer mortality statistics](#). Accessed September 2015.
3. Cancer Research UK (2014) [Breast cancer survival statistics](#). Accessed September 2015.
4. Cancer Research UK (2015) [Breast cancer incidence statistics](#). Accessed September 2015.
5. NICE (2009) [Costing report for clinical guideline 81: advanced breast cancer](#). Accessed September 2015.
6. Dewis R and Gribbin J (2009) [Breast cancer: diagnosis and treatment, an assessment of need](#). Cardiff: National Collaborating Centre for Cancer. Accessed October 2015.