NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Ribociclib with fulvestrant for treating hormone receptor-positive, HER2-negative advanced breast cancer (CDF review of TA593)

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of ribociclib 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 2016 in England, around 45,960 people were diagnosed with breast cancer[1]. In 2016 there were 9,685 deaths from breast cancer in England[2]. The 1-year survival rate for adults with metastatic breast cancer in England is 63%[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].

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 (hormone receptor status or 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. 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 women 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

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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. 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

Ribociclib (Kisqali, Novartis) is a selective cyclin-dependent-kinase 4 and 6 (CDK4/6) inhibitor. When either of these two proteins are activated they can cause the cancer cells to grow and divide too quickly. It is administered orally.

Ribociclib in combination with fulvestrant does not currently have a marketing authorisation in the UK for treating hormone receptor-positive, HER2-negative breast cancer. It has been studied in clinical trials in combination with fulvestrant, compared with placebo, in the treatment of men and postmenopausal women with hormone receptor positive, HER2-negative, advanced breast cancer (including people treated with an endocrine therapy in the adjuvant setting) who have received no or only one line of prior endocrine treatment in the advanced setting.

Ribociclib in combination with an aromatase inhibitor has a marketing authorisation for the treatment of postmenopausal women with hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer as initial endocrine-based therapy.

Intervention(s)	Ribociclib in combination with fulvestrant
Population(s)	• People with untreated advanced hormone-receptor positive HER2-negative breast cancer • People with advanced hormone-receptor positive HER2-negative breast cancer that has progressed after prior endocrine therapy

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Comparators	For people with untreated advanced hormone-receptor positive HER2-negative breast cancer: • Palbociclib in combination with an aromatase inhibitor • Ribociclib in combination with an aromatase inhibitor • Tamoxifen (in accordance with NICE guidance CG81) For people with advanced hormone-receptor positive HER2-negative breast cancer that has progressed after one line of prior endocrine therapy: • Exemestane • Everolimus and exemestane • Tamoxifen • Fulvestrant • Chemotherapy (in accordance with NICE guidance CG81)
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • adverse effects of treatment • health-related quality of life.

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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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out. 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 Pathways	Related Technology Appraisals: Fulvestrant for untreated locally advanced or metastatic oestrogen-receptor positive breast cancer (2018). NICE technology appraisal 503. Next review date to be confirmed. Ribociclib in combination with an aromatase inhibitor for previously untreated advanced or metastatic hormone receptor-positive, HER2-negative breast cancer (2017). NICE technology appraisal 496. Next review date December 2020 Palbociclib in combination with an aromatase inhibitor for previously untreated metastatic, hormone receptor-positive, HER2-negative breast cancer (2017). NICE technology appraisal 495. Next review date December 2020 Everolimus with exemestane for treating advanced breast cancer after endocrine therapy (2016) NICE technology appraisal 421. Next review December 2019. Fulvestrant for the treatment of locally advanced or metastatic breast cancer (2011). NICE Technology

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	Appraisal 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. Appraisals in development (including suspended appraisals): Abemaciclib monotherapy for treating advanced hormone-receptor positive, HER2-negative breast cancer after endocrine therapy and chemotherapy Proposed NICE technology appraisal [ID1347]. Publication date to be confirmed Abemaciclib with fulvestrant for treating advanced hormone-receptor positive, HER2-negative breast cancer after endocrine therapy Proposed NICE technology appraisal [ID1339]. Publication date to be confirmed. Abemaciclib with an aromatase inhibitor for untreated advanced hormone-receptor positive, HER2-negative breast cancer Proposed NICE technology appraisal [ID1227]. Expected publication date: 20 February 2019. Palbociclib for treating hormone-receptor positive, HER2-negative breast cancer. NICE technology appraisal guidance [ID916]. Suspended. Related Guidelines: Advanced breast cancer: diagnosis and treatment (2009, updated 2017). NICE guideline CG81. Review date August 2017. 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. Next review to be scheduled. Related Quality Standards: Breast cancer (2011, updated 2016). NICE quality standard 12. Related NICE Pathways: Advanced breast cancer (2017) NICE Pathway Familial breast cancer (2013) NICE Pathway
Related National Policy	NHS England (2017) 'Manual for Prescribed Specialised Services'. Chapter 105, Specialist Cancer services

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	(adults) Department of Health (2016) NHS Outcomes Framework 2016-2017. Domains 1 and 2.

References

1 Office for National Statistics (2016) Cancer registration statistics, England, 2016. Accessed June 2018.

2 Office for National Statistics (2017) Mortality statistics – underlying cause, sex and age. Accessed December 20173 Cancer Research UK (2014) Breast cancer survival statistics. Accessed November 2017.

4 Cancer Research UK (2014) Breast cancer incidence statistics. Accessed November 2017.

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

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