NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Ribociclib in combination with endocrine therapy and goserelin for previously untreated hormone receptor-positive, HER2-negative advanced breast cancer in premenopausal women

Draft scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of ribociclib within its marketing authorisation for previously untreated advanced, hormone receptor-positive, HER2-negative breast cancer in premenopausal women.

Background

Breast cancer arises from the tissues of the ducts or lobules of the breast. 'Locally advanced' cancer describes tumours that are larger than 5 cm in size, or have grown into the skin or muscle of the chest or nearby lymph nodes. Metastatic breast cancer describes disease that has spread to another part of the body, such as the bones, liver, or lungs.

In 2014 in England, around 46,417 people were diagnosed with breast cancer, and there were approximately 9,554 deaths from breast cancer[1,2]. The 5-year survival rate for people with metastatic breast cancer in England is 15%[3]. Approximately 13% of women with invasive breast cancers have locally advanced or metastatic disease when they are diagnosed[4], it has been estimated that 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 locally advanced and metastatic breast cancer aim to relieve symptoms, prolong survival and maintain a good quality of life with minimal 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.

For people with advanced or metastatic hormone receptor-positive breast cancer, NICE Clinical Guideline 81 (CG81) recommends tamoxifen and ovarian suppression (e.g. goserelin) as first-line treatment for premenopausal and perimenopausal women with estrogen receptor-positive advanced breast cancer not previously treated with tamoxifen, and ovarian suppression is recommended for premenopausal and perimenopausal women who have previously been treated with tamoxifen and then experience disease progression.

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 taken orally.

Ribociclib does not currently have a marketing authorisation in the UK for premenopausal women. It has been studied in a clinical trial in combination with goserelin, and tamoxifen or a non-steroidal aromatase inhibitor (letrozole or anastrozole), in premenopausal and perimenopausal women with hormone receptor positive, HER2-negative advanced breast cancer; in patients who have received no prior therapy for advanced disease.

Intervention(s)	Ribociclib in combination with goserelin and • tamoxifen or • a non-steroidal aromatase inhibitor (letrozole or anastrozole)
Population(s)	Premenopausal women with previously untreated advanced hormone receptor positive, HER2 negative breast cancer.
Comparators	Goserelin in combination with • tamoxifen or • a non-steroidal aromatase inhibitor (letrozole or anastrozole)
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 intervention or 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 Guidelines: Advanced breast cancer: diagnosis and treatment (2009). NICE guideline 81 This guidance replaces previous Technology Appraisals No. 30, 54 and 62. Last updated in 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). NICE guideline CG164. Last updated in March 2017. Related Quality Standards: 'Breast cancer' (2011) NICE quality standard 12. Last updated in June 2016. 'Related NICE Pathways: Advanced breast cancer (2017) NICE pathway Familial breast cancer (2017) NICE pathway
Related National Policy	Department of Health (2016) 'NHS Outcomes Framework. Domain 1. NHS England (2016) 'Manual for Prescribed Specialised Services'. Chapter 105, Specialist Cancer services (adults)

Questions for consultation

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

- Is ovarian suppression (goserelin) and a non-steroidal aromatase inhibitor (letrozole or anastrozole) used for untreated hormone receptor-positive, HER2-negative advanced breast cancer in premenopausal women?
- In addition to goserelin, should any other ovarian suppression treatments be considered in the scope?
- Have all relevant comparators for ribociclib been included in the scope?

Should perimenopausal people be included in the scope?

Are the outcomes listed appropriate?

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

Where do you consider ribociclib will fit into the existing NICE pathways, 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 ribociclib 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 ribociclib 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 ribociclib 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).

References

1. Office for National Statistics (2014) Cancer registration statistics, England, 2014. Accessed December 2016.

2. Cancer Research UK (2014) Breast cancer mortality statistics. Accessed September 2017.

3. Cancer Research UK (2014) Breast cancer survival statistics. Accessed September 2017.

4. Cancer Research UK (2015) Breast cancer incidence statistics. Accessed September 2017.

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