NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Pertuzumab for the neoadjuvant treatment of HER2-positive breast cancer

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of pertuzumab within its marketing authorisation for the neoadjuvant treatment of human epidermal growth factor receptor 2 (HER2) positive breast cancer.

Background

Breast cancer is described as 'early' if it is restricted to the breast, or the breast and nearby lymph nodes, and has not spread to other parts of the body. It is described as 'locally advanced' if the cancer in a large part of the breast but has not spread to other parts of the body, and described as 'advanced' if it has spread to other parts of the body and cannot be completely removed by surgery. Inflammatory breast cancer is a rare but aggressive type of breast cancer in which cancer cells grow along, and block the lymph nodes in the skin of the breast causing it to become inflamed and swollen. Human epidermal growth factor receptor 2 (HER2) is a receptor for a growth factor which occurs naturally in the body. When human epidermal growth factor attaches itself to HER2 receptors on breast cancer cells, it can stimulate the cells to divide and grow. Some breast cancer cells have more HER2 receptors than others. In this case, the tumour is described as being HER2-positive.

In 2011 in England, there were approximately 42,000 diagnoses of breast cancer with an estimated 10,000 deaths. It is estimated that approximately 1 in 5 women with breast cancer will have HER2-positive tumours. Men are less likely to have HER-2 positive breast cancers[2].

NICE clinical guideline 80 recommends that early breast cancer can be treated with surgery (to remove the tumour) followed by chemotherapy (adjuvant) to reduce the risk of the cancer coming back. NICE clinical guideline 80 also recommends that systemic therapy could be offered before surgery (neoadjuvant) to people with early invasive, locally advanced or inflammatory breast cancer who are considering breast conserving surgery that is not advisable at presentation.

The technology

Pertuzumab (Perjeta, Roche Products) is a recombinant monoclonal antibody which targets HER2- positive breast tumours. It interrupts the activation of the HER2 intracellular signalling pathway, leading to cell growth arrest and apoptosis. Pertuzumab is administered by intravenous infusion.

Pertuzumab does not currently have a marketing authorisation in the UK for the neoadjuvant treatment of HER-2 positive breast cancer. It has been studied in women with operable, locally advanced or inflammatory early breast cancer in combination with trastuzumab and/or docetaxel in a phase 2 clinical trial compared with trastuzumab and/or docetaxel. Following treatment all eligible women underwent surgery and if suitable received fluorouracil, epirubicin and cyclophosphamide (FEC regimen) chemotherapy. In addition, concomitant treatment with trastuzumab was given for 1 year after surgery.

Pertuzumab has a UK marketing authorisation for use in combination with trastuzumab and docetaxel in adult patients with HER2-positive metastatic or locally recurrent unresectable breast cancer who have not received previous anti-HER2 therapy or chemotherapy for their metastatic disease.

Intervention(s)	Neoadjuvant pertuzumab in combination with trastuzumab and docetaxel.
Population(s)	Adults with HER2-positive, locally advanced, inflammatory, or early stage breast cancer.
Comparators	• Standard neoadjuvant therapy without pertuzumab for HER-2 positive breast cancer. • No neoadjuvant systemic therapy.
Outcomes	The outcome measures to be considered include: • overall survival • progression free survival • response rate • surgical outcomes • pathological complete response • 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. Biosimilars are not expected to be in established NHS practice at the time of appraisal and are not included as comparators.

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: Appraisals in development: 'Pertuzumab in combination with trastuzumab and docetaxel for the treatment of HER2 positive metastatic or locally recurrent unresectable breast cancer, which has not been previously treated, or has relapsed after adjuvant therapy. NICE technology appraisals guidance. [ID523]. Publication date to be confirmed. Related Guidelines: 'Breast cancer (early & locally advanced): diagnosis and treatment' (2009) NICE guideline 80. Review date: June 2015. Related Quality Standards: 'Breast cancer quality standard' (2011) NICE quality standard 12. Related NICE Pathways: Early and locally advanced breast cancer (2015) NICE pathway: http://pathways.nice.org.uk/pathways/early-and-locally-advanced-breast-cancer
Related National Policy	Cancer Drugs Fund, NHS England. Updated March 2015. http://www.england.nhs.uk/wp-content/uploads/2015/03/ncdf-list-mar-15.pdf Department of Health, NHS Outcomes Framework 2014-2015, Nov 2013. Domains 1-5. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf

Questions for consultation

Have all relevant comparators for pertuzumab been included in the scope?

- Which neoadjuvant treatments are considered to be established clinical practice in the NHS for people with HER2-positive, locally advanced, inflammatory, or early stage breast cancer?

Who would be considered for neoadjuvant therapy in clinical practice?

Are there any subgroups of people in whom pertuzumab is expected to be more clinically effective and cost effective or other groups that should be examined separately? For example people with locally advanced or inflammatory breast cancer or those with oestrogen receptor positive tumours.

Where do you consider pertuzumab will fit into the existing NICE pathway for early and locally 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 pertuzumab 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 pertuzumab 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 pertuzumab 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. Cancer Research UK (2011). Breast cancer incidence statistics. Accessed April 2015.

2. Macmillan. Information and support: HER-2 positive breast cancer. Accessed April 2015.