NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Pertuzumab for the neoadjuvant treatment of HER2-positive breast cancer

Final scope

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 (clinical stages 1 and 2). It is described as 'locally advanced' if the cancer is in a large part of the breast (more than 5 cm) but has not spread to other parts of the body (clinical stage 3), and described as 'advanced' if it has spread to other parts of the body and cannot be completely removed by surgery (clinical stage 4).

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. Inflammatory breast cancer affects the breast differently and usually the whole breast and the overlying skin are affected (clinical stage 3 or 4).

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[1]. It is estimated that approximately 15-25% of 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 (recurrence).

Locally advanced and inflammatory breast cancers are considered to have a high-risk of recurrence. In early stage breast cancer, risk assessment for recurrence depends upon, tumour size, grade, hormone receptor status and

lymph node involvement. 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 commonly used neoadjuvant therapy for HER-2 positive breast cancer includes fluorouracil epirubicin and cyclophosphamide followed by docetaxel plus trastuzumab. For people who cannot have an anthracycline (epirubicin) the neoadjuvant therapy comprises trastuzumab, docetaxel and carboplatin.

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 has a marketing authorisation in the UK 'in combination with trastuzumab and chemotherapy for the neoadjuvant treatment of adult patients with HER-2 positive, locally advanced, inflammatory, or early stage breast cancer at high risk of recurrence'.

Intervention(s)	Neoadjuvant pertuzumab in combination with trastuzumab and chemotherapy.
Population(s)	Adults with HER2-positive breast cancer which is either; • locally advanced, or • inflammatory, or • early stage (at a high-risk of recurrence).
Comparators	Standard neoadjuvant therapy without pertuzumab for HER-2 positive breast cancer.
Outcomes	The outcome measures to be considered include: • overall survival • disease free survival • 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.
Other considerations	If the evidence allows the subgroups indicated in the 'population' section will be considered separately. 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: '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

References

1. Cancer Research UK (2011). Breast cancer incidence statistics. Accessed November 2015.

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