NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Trastuzumab emtansine for adjuvant treatment of HER2-positive early breast cancer ID1516

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of trastuzumab emtansine within its marketing authorisation for treating human epidermal growth factor receptor 2 (HER2) positive early breast cancer in the adjuvant setting.

Background

Breast cancer arises from the tissues of the ducts or lobules of the breast. 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 is in a large part of the breast (more than 5 cm) but has not spread to other parts of the body.

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 2016, there were approximately 45,960 new diagnoses of breast cancer in England[1]. It is estimated that approximately 15-25% of women with breast cancer will have HER2-positive tumours. Men are less likely to have HER2 positive breast cancers[2].

Neoadjuvant therapy is considered as an option to reduce tumour size prior to surgery. TA424 recommends pertuzumab with trastuzumab and chemotherapy as a neoadjuvant treatment of HER2-positive, locally advanced, inflammatory or early-stage breast at high risk of recurrence. The decision about whether to have adjuvant therapy is based on an assessment of the risk of the cancer coming back and the potential benefits and side effects of the treatment. NICE guideline 101 recommends offering adjuvant trastuzumab for 1 year in combination with surgery, chemotherapy and radiotherapy as appropriate. People with oestrogen receptor-positive breast cancer at medium to high risk of recurrence are offered adjuvant endocrine therapy (usually an aromatase inhibitor). TA569 recommends pertuzumab, with trastuzumab and chemotherapy for the adjuvant treatment of HER2-positive early stage breast cancer in adults, who have a lymph node-positive disease.

The technology

Trastuzumab emtansine (Kadcyla, Roche Products) is an antibody-drug conjugate. This combines anti-HER activity with targeted intracellular delivery. Trastuzumab emtansine is administered via intravenous infusion.

Trastuzumab emtansine does not currently have a UK marketing authorisation for treating HER2-positive breast cancer in the adjuvant setting. It has been studied in a clinical trial, compared with trastuzumab, in adults who have residual tumour in the breast or axillary lymph nodes following neoadjuvant therapy containing a taxane (with or without anthracycline) and trastuzumab.

Trastuzumab emtansine has a UK marketing authorisation as a single agent for treating HER2‑positive, unresectable, locally advanced or metastatic breast cancer in adults who previously received trastuzumab and a taxane, separately or in combination. Patients should have either received prior therapy for locally advanced or metastatic disease, or developed disease recurrence during or within 6 months of completing adjuvant therapy.

Intervention(s)	Trastuzumab emtansine
Population(s)	Adults with HER2-positive early breast cancer who have residual disease following neoadjuvant therapy containing a taxane (with or without anthracycline) and HER2-targeted therapy.
Comparators	• Standard adjuvant therapies including trastuzumab For people with node-positive disease • Pertuzumab in combination with trastuzumab and chemotherapy
Outcomes	The outcome measures to be considered include: • overall survival • disease-free survival • 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 commercial arrangements for the intervention, comparator and subsequent treatment 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. If evidence allows, the following subgroups will be considered separately: • prior neoadjuvant therapy including trastuzumab (with no prior pertuzumab therapy), and • prior neoadjuvant therapy including pertuzumab with trastuzumab. The availability and cost of biosimilar products should be taken into account.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: Pertuzumab for adjuvant treatment of early HER2-positive breast cancer (2019) NICE technology appraisal guidance 569. Trastuzumab emtansine for treating HER2-positive advanced breast cancer after trastuzumab and a taxane (2017) NICE technology appraisal guidance 458. Pertuzumab for the neoadjuvant treatment of HER2-positive breast cancer (2016) NICE technology appraisal guidance 424. Appraisals in development (including suspended appraisals) Neratinib for treating early HER2-positive breast cancer after adjuvant trastuzumab

	[ID981] Publication expected October 2019 Related Guidelines: Early and locally advanced breast cancer: diagnosis and management (2018) NICE clinical guideline NG101 Related Quality Standards: • Breast cancer (2011, updated 2016) NICE quality standard QS12 Related NICE Pathways: • Early and locally advanced breast cancer NICE pathway • Familial breast cancer NICE pathway
Related National Policy	NHS England, Manual for prescribed specialised services 2017/18: 105 – Specialist cancer services (adults) Department of Health, Improving Outcomes: A Strategy for Cancer, fourth annual report, Dec 2014 Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1 and 2.

References

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

2. Macmillan. Information and support: HER-2 positive breast cancer. Accessed November 2018.

