NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

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

Draft scope

Draft 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 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 HER-2 positive breast cancers[2].

NICE clinical guideline 101 recommends offering adjuvant trastuzumab for people with HER2-positive invasive breast cancer who need adjuvant therapy to reduce the risk of the cancer coming back. 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. Adjuvant trastuzumab is given for 1 year or until disease recurrence, whichever is the shorter period. People with oestrogen receptor-positive breast cancer at medium to high risk of recurrence are offered adjuvant endocrine therapy (usually an aromatase inhibitor).

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)	People with HER2-positive breast cancer who have residual disease following neoadjuvant therapy containing a taxane (with or without anthracycline) and trastuzumab
Comparators	• Trastuzumab • Pertuzumab in combination with trastuzumab and chemotherapy (subject to NICE guidance)
Outcomes	The outcome measures to be considered include: • overall survival • disease 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 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. The availability and cost of biosimilar products should be taken into account.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: 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) Pertuzumab for adjuvant treatment of early HER2-positive breast cancer [ID1192]. Publication expected March 2019. 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 Gene expression profiling and expanded immunohistochemistry tests for guiding adjuvant chemotherapy decisions in early breast cancer management: MammaPrint, Oncotype DX, IHC4 and Mammostrat (2013) NICE diagnostic guidance 10. 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.

Questions for consultation

Have all relevant comparators for trastuzumab emtansine been included in the scope?

- Which treatments are considered to be established clinical practice in the NHS for HER2-positive breast cancer in the adjuvant setting?
- Would pertuzumab in combination with trastuzumab and chemotherapy (subject to positive guidance) be the only relevant comparator for people with lymph-node-positive disease?

Pertuzumab in combination with trastuzumab and chemotherapy is recommended as an option for the neoadjuvant treatment of adults with HER2-positive, locally advanced, inflammatory or early-stage breast cancer at high risk of recurrence neoadjuvant therapy (TA424).

- Would a treatment with trastuzumab emtansine in the adjuvant setting be considered following a prior neoadjuvant treatment recommended in TA424? Or would trastuzumab emtansine be used only after prior neoadjuvant treatment without pertuzumab?

Are the outcomes listed appropriate?

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

Where do you consider trastuzumab emtansine will fit into the existing NICE pathway, 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 the treatments will be licenced;

- 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 trastuzumab emtansine 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 trastuzumab emtansine 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).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?

- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?

- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?

- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

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.

