NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Etirinotecan pegol for treating locally advanced or metastatic breast cancer after chemotherapy

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of etirinotecan pegol within its marketing authorisation for treating locally advanced or metastatic breast cancer previously treated with chemotherapy.

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, and may 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.

Over 44,800 people were diagnosed with breast cancer in England in 2013, and there were approximately 9800 deaths from breast cancer in 2012[1,2]. The 5-year survival rate for people with metastatic breast cancer in England is 15%[3]. Approximately 17% of women with invasive breast cancers have locally advanced or metastatic disease when they are diagnosed[4], and around 35% of people with early or locally advanced disease will progress to metastatic breast cancer[5,6].

Current treatments for metastatic breast cancer aim to relieve symptoms, prolong survival and maintain a good quality of life with few 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; options include endocrine therapies, biological therapies and chemotherapy. For people having chemotherapy for advanced breast cancer, NICE clinical guideline 81 (CG81) recommends anthracycline-based regimens as the initial treatment, followed by sequential lines of treatment with docetaxel, capecitabine and vinorelbine. For people whose disease progresses after these treatments, options including eribulin (available through the Cancer Drugs Fund), paclitaxel, gemcitabine, carboplatin and best supportive care may be considered in clinical practice.

The technology

Etirinotecan pegol (brand name unknown; Nektar Therapeutics) is a chemotherapy drug that consists of the topoisomerase-I inhibitor irinotecan bound to polyethylene glycol. It is broken down in the body to release the active part of irinotecan, which destroys cancer cells by disrupting DNA replication. Etirinotecan pegol is administered as an intravenous infusion.

Etirinotecan pegol does not currently have a marketing authorisation in the UK. It has been studied in a clinical trial, compared with single-agent chemotherapy, for treating locally advanced or metastatic breast cancer in people who have had previous treatment with an anthracycline, a taxane and capecitabine.

Intervention(s)	Etirinotecan pegol
Population(s)	Adults with locally advanced or metastatic breast cancer, who have had previous treatment with an anthracycline, a taxane and capecitabine
Comparators	• Eribulin (not recommended by NICE but available through the CDF) • Vinorelbine • Paclitaxel • Gemcitabine • Carboplatin • Best supportive care
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.

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: • Eribulin for the treatment of locally advanced or metastatic breast cancer (2012). NICE Technology Appraisal 250. Static list. Appraisals in development (including suspended appraisals) • Trastuzumab emtansine for the treatment of unresectable locally advanced or metastatic breast cancer after treatment with trastuzumab and a taxane. NICE Technology Appraisal guidance [ID608]. Publication date to be confirmed. • Sunitinib in combination with capecitabine within its licensed indication for the treatment of advanced and/or metastatic breast cancer. NICE Technology Appraisal guidance [ID319]. Suspended. • Ixabepilone for locally advanced or metastatic breast cancer. NICE Technology Appraisal guidance [ID377]. Suspended. • Lapatinib for breast cancer (for use in women with previously treated advanced or metastatic breast cancer). NICE Technology Appraisal guidance [ID20]. Suspended. • Bevacizumab for the second line treatment of HER2 negative metastatic breast cancer. NICE Technology Appraisal guidance [ID488]. Suspended. Related Guidelines: • Advanced breast cancer: diagnosis and treatment (2009, updated 2014). NICE guideline 81. Review date December 2015. • Early and locally advanced breast cancer: diagnosis and treatment (2009, updated 2014). NICE guideline 80. Review date December 2015. Related Quality Standards: • Quality Standard No. 12, September 2011, 'Breast cancer'. Update in progress, publication expected

	June 2016. Related NICE Pathways: • NICE pathway: Advanced breast cancer, Pathway created June 2014: http://pathways.nice.org.uk/pathways/advanced-breast-cancer
Related National Policy	NHS England, Manual for prescribed specialised services 2013/14: 105 – Specialist cancer services (adults). http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf Department of Health, Improving Outcomes: A Strategy for Cancer, third annual report, Dec 2013 https://www.gov.uk/government/publications/the-national-cancer-strategy-3rd-annual-report--2 Department of Health, NHS Outcomes Framework 2015-2016, Dec 2014. Domains 1, 2, 4 and 5. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385749/NHS_Outcomes_Framework.pdf

Questions for consultation

Have all relevant comparators for etirinotecan pegol been included in the scope?

- Which treatments are considered to be established clinical practice in the NHS for locally advanced or metastatic breast cancer that has been previously treated with an anthracycline, a taxane and capecitabine?
- Are any other chemotherapy options (such as cyclophosphamide-based regimens) considered in clinical practice?
- Is chemotherapy based on single-agent or combination regimens in this population?
- How should best supportive care be defined?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom etirinotecan pegol is expected to be more clinically effective and cost effective or other groups that should be examined separately? Should consideration be given to subgroups based on biological markers (such as HER2 or hormone receptors) or previous treatment?

Where do you consider etirinotecan pegol will fit into the existing NICE pathway, 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 etirinotecan pegol 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 etirinotecan pegol 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 etirinotecan pegol 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. Office for National Statistics (2015) Cancer registration statistics, England, 2013. Accessed September 2015.

2. Cancer Research UK (2014) Breast cancer mortality statistics. Accessed September 2015.

3. Cancer Research UK (2014) Breast cancer survival statistics. Accessed September 2015.

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

5. NICE (2009) Costing report for clinical guideline 81: advanced breast cancer. Accessed September 2015.

6. Dewis R and Gribbin J (2009) Breast cancer: diagnosis and treatment, an assessment of need. Cardiff: National Collaborating Centre for Cancer. Accessed October 2015.