

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Single Technology Appraisal**

**Etirinotecan pegol for treating breast cancer with brain metastases**

**Remit/appraisal objective**

To appraise the clinical and cost effectiveness of etirinotecan pegol within its marketing authorisation for treating metastatic breast cancer with brain metastases.

**Background**

Breast cancer arises from the tissues of the ducts or lobules of the breast. Metastatic breast cancer describes tumours that have spread to another part of the body, such as the bones, liver or brain.

Over 44,800 people were diagnosed with breast cancer in England in 2013, and there were approximately 9800 deaths from breast cancer in 2012<sup>1,2</sup>. The 5-year survival rate for people with metastatic breast cancer in England is 15%<sup>3</sup>. Approximately 5% of women with invasive breast cancers have metastatic disease when they are diagnosed<sup>4</sup>, and around 35% of people with early or locally advanced disease will progress to metastatic breast cancer<sup>5,6</sup>. An estimated 5% of people with breast cancer, and 10–16% of those with advanced disease, develop brain metastases<sup>7,8</sup>.

Current treatments for metastatic breast cancer aim to relieve symptoms, prolong survival and maintain a good quality of life with few adverse events. Treatment depends 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 (subject to ongoing NICE appraisal), gemcitabine, carboplatin and best supportive care may be considered in clinical practice. For people with brain metastases, CG81 recommends surgery and/or whole-brain radiotherapy; in clinical practice, stereotactic radiotherapy and chemotherapy may also be considered.

**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.

<b>Intervention(s)</b>	Etirinotecan pegol
<b>Population(s)</b>	Adults with advanced breast cancer with brain metastases who have received prior anthracycline, taxane, and capecitabine therapy, unless these treatments were not suitable.
<b>Comparators</b>	<ul style="list-style-type: none"> <li>• eribulin (subject to ongoing NICE appraisal),</li> <li>• vinorelbine,</li> <li>• gemcitabine,</li> <li>• carboplatin</li> </ul>
<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• overall survival</li> <li>• progression free survival</li> <li>• response rate</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul>
<b>Economic analysis</b>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any patient access schemes for the intervention or comparator technologies will be taken into account.</p>

<b>Other considerations</b>	<p>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.</p>
<b>Related NICE recommendations and NICE Pathways</b>	<p>Related Technology Appraisals:</p> <ul style="list-style-type: none"> <li>• <a href="#">Trastuzumab emtansine for the treatment of unresectable locally advanced or metastatic breast cancer after treatment with trastuzumab and a taxane</a> (2015). NICE Technology Appraisal 371. Review date Dec 2018.</li> <li>• <a href="#">Everolimus in combination with exemestane for treating advanced HER2-negative hormone-receptor-positive breast cancer after endocrine therapy</a> (2013). NICE Technology Appraisal 295. Review proposal in progress.</li> <li>• <a href="#">Breast cancer (locally advanced, metastatic) - eribulin (after chemotherapy)</a> [ID964] Under ongoing review.</li> <li>• <a href="#">Eribulin for treating locally advanced or metastatic breast cancer after one prior chemotherapy regimen</a> [ID1072] Under ongoing review</li> <li>• <a href="#">Eribulin for treating locally advanced or metastatic breast cancer after 2 or more chemotherapy regimen</a> [review of NICE Technology Appraisal 250, ID964] Under ongoing review</li> <li>• <a href="#">Fulvestrant for the treatment of locally advanced or metastatic breast cancer</a> (2011). NICE Technology Appraisal 239. Static list.</li> <li>• <a href="#">Gemcitabine for the treatment of metastatic breast cancer</a> (2007). NICE Technology Appraisal 116. Static list.</li> </ul> <p>Related Guidelines:</p> <ul style="list-style-type: none"> <li>• <a href="#">Advanced breast cancer: diagnosis and treatment</a> (2009, updated 2014). NICE guideline 81. Update in progress publication expected June 2017.</li> <li>• <a href="#">Early and locally advanced breast cancer: diagnosis and treatment</a> (2009, updated 2014). NICE guideline 80. Update in progress publication expected July 2018.</li> </ul> <p>Guidelines in development</p>

	<ul style="list-style-type: none"> <li>• <a href="#">Primary brain tumours and cerebral metastases in adults</a>. Publication expected July 2018.</li> </ul> <p>Related Quality Standards:</p> <ul style="list-style-type: none"> <li>• Quality Standard No. 12, September 2011, 'Breast cancer'. Updated June 2016. <a href="https://www.nice.org.uk/guidance/qs12/chapter/usin-g-the-quality-standard">https://www.nice.org.uk/guidance/qs12/chapter/usin-g-the-quality-standard</a></li> </ul> <p>Related NICE Pathways:</p> <ul style="list-style-type: none"> <li>• NICE pathway: Advanced breast cancer, Pathway created June 2014 Updated June 2016. <a href="http://pathways.nice.org.uk/pathways/advanced-breast-cancer">http://pathways.nice.org.uk/pathways/advanced-breast-cancer</a></li> </ul>
<b>Related National Policy</b>	<p>NHS England, Manual for prescribed specialised services 2013/14: 105 – Specialist cancer services (adults). <a href="http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf">http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf</a></p> <p>Department of Health, Improving Outcomes: A Strategy for Cancer, 4th annual report, Dec 2014 <a href="https://www.gov.uk/government/publications/the-national-cancer-strategy-4th-annual-report">https://www.gov.uk/government/publications/the-national-cancer-strategy-4th-annual-report</a></p> <p>Department of Health, NHS Outcomes Framework 2015-2016, Dec 2014. Domains 1, 2, 4 and 5. <a href="https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385749/NHS_Outcomes_Framework.pdf">https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385749/NHS_Outcomes_Framework.pdf</a></p>

## References

1. Office for National Statistics (2015) [Cancer registration statistics, England, 2013](#). Accessed January 2016.
2. Cancer Research UK (2014) [Breast cancer mortality statistics](#). Accessed January 2016.
3. Cancer Research UK (2014) [Breast cancer survival statistics](#). Accessed January 2016.
4. Cancer Research UK (2015) [Breast cancer incidence statistics](#). Accessed January 2016.
5. NICE (2009) [Costing report for clinical guideline 81: advanced breast cancer](#). Accessed January 2016.

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