A review of TA250 should be planned into the appraisal work programme as a single technology appraisal (STA). The consultation responses to the review proposal highlighted the following aspects that had not been taken in to account in the review proposal paper, when proposing to place TA250 on the static list:

- The more mature data from the EMBRACE trial, which may strengthen the economic analysis by reducing the uncertainty associated with the extrapolation of overall survival in the original appraisal.
- TA250 recommended that health-related quality of life studies comparing eribulin with vinorelbine and capecitabine should be conducted. A study comparing eribulin with capecitabine for locally advanced or metastatic breast cancer treated before with anthracyclines and taxanes (Study 301) has reported health-related quality of life results, which can be used in the economic analysis.
- A new patient access scheme is proposed, which, if approved, could improve the cost effectiveness of eribulin.
- A new 3-ml vial is now available; this may improve the cost effectiveness of eribulin by reducing wastage.

In light of the above, it is proposed to seek a broad remit covering the full licensed indication for eribulin for breast cancer, and carry out an STA that includes the review of TA250 (third- or subsequent-line treatment) together with an appraisal of the extended indication (second-line treatment), which is currently progressing separately through the scoping process as a proposed STA.

1. Background

This guidance was issued in April 2012.

At the GE meeting of 28 October 2014 it was agreed that we would consult on the recommendations made in the GE proposal paper. A four week consultation has been conducted with consultees and commentators and the responses are presented below.
2. Proposal put to consultees and commentators
The guidance should be transferred to the ‘static guidance list’.

3. Rationale for selecting this proposal
There has been no significant new evidence identified that is likely to lead to a change in the current recommendations in TA250. There is 1 ongoing randomised controlled trial relevant to this appraisal comparing eribulin with vinorelbine. At this stage, it is considered appropriate to move TA250 to the ‘static guidance list’, with a flag to consider the impact of the ongoing trial as necessary.

4. Summary of consultee and commentator responses
Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

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<tr>
<th>Respondent: Breakthrough Breast Cancer</th>
<th>Comment from Technology Appraisals</th>
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<td>Response to proposal: Delay decision</td>
<td>Response note.</td>
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<td>TA 250 refers specifically to the use of eribulin for the treatment of patients who have previously had at least two chemotherapeutic regimens for advance disease. As NICE is no doubt aware, eribulin is currently available through the Cancer Drugs Fund for this indication. NICE will also be aware that at the next meeting of the Cancer Drugs Fund panel, eribulin for this indication will be reassessed to consider any new evidence and decide whether the drug should remain available through the Cancer Drugs Fund. In addition to this, the Cancer Drugs Fund panel will also be considering whether eribulin should be made available on the Fund as a second line treatment. We appreciate that this is a slightly different indication and that NICE operates independently to the Cancer Drugs Fund. However, neither system can exist in isolation and the fact that eribulin has been submitted to the Cancer Drugs Fund panel for a new indication suggests that there is some new evidence surrounding the effectiveness of the drug. We would therefore suggest that NICE delays making a decision on this until after the Cancer Drugs Fund panel has made a decision to establish whether the new evidence...</td>
<td>A review of TA250 should be planned into the appraisal work programme as an STA. It is proposed to seek a broad remit covering the full licensed indication for eribulin for breast cancer, and carry out an STA that includes the review of TA250 (third- or subsequent-line treatment) together with an appraisal of the extended indication (second-line treatment).</td>
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presented to the panel will impact on TA250. If the evidence for eribulin as a second line treatment is considered strong enough to make the drug available on the Cancer Drugs Fund, NICE may also wish to consider carrying out an additional technology appraisal of eribulin in this indication to establish whether it should be available routinely on the NHS.

Respondent: Pierre Fabre  
Response to proposal: No comment  
We have no further comments.

Respondent: Royal College of Nursing  
Response to proposal: No comment  
Nursing working in this area of health have reviewed this proposal and have no comments to submit at this present time.

Respondent: Royal College of Physicians  
Response to proposal: Agree  
We agree with the proposal to move the guidance to the static list due to the absence of new data relevant to TAG250. Our experts note the recent licence extension of eribulin to a second line agent for metastatic breast cancer and look forward to commenting on new guidance in relation to the revised indication in due course.

Comment from Technology Appraisals  
Response noted.

Comment from Technology Appraisals  
Response noted.

Comment from Technology Appraisals  
Response noted.

A review of TA250 should be planned into the appraisal work programme as an STA. It is proposed to seek a broad remit covering the full licensed indication for eribulin for breast cancer, and carry out an STA that includes the review of TA250 (third- or subsequent-line treatment) together with an appraisal of the extended indication (second-line treatment).
Respondent: Eisai
Response to proposal: Disagree

Since the last NICE assessment (TA250), significant new evidence has emerged on eribulin:

1. Overall Survival
As is common in cancer trials, more mature data has been collected from the pivotal Phase III trial (EMBRACE).

Updated results for overall survival (OS) after 95% of subject deaths had occurred (724 deaths in 762 enrolled patients) is now available from the EMBRACE trial. TA 250 was based on the cut off data when 55% and 77% of deaths had occurred.

As a result of the less mature survival data, extrapolation of the overall survival results was required for the economic case and this created uncertainty in the results and the generated ICERs in TA250.

Now with very mature data this uncertainty in relation to the overall survival is removed.

This means that eribulin could potentially also meet the end of life criteria.

2. Restricted Indication
Furthermore since eribulin was launched in the UK in April 2011, real life data and audits collected from a number of cancer centres such as the Marsden, Christie and Sheffield show that > 80% of patients have received capecitabine prior to starting eribulin (1, 2, 3). In light of this, a defined population and in keeping with clinical practice is derived for the economic case. In the EMBRACE trial 74% of the trial participants had received capecitabine. (4). However in TA250 eribulin was only evaluated vs vinorelbine by breaking down the TPC arm of the trial in the post capecitabine population. This was criticised by the appraisal committee for the very small number of patients in the comparator.

Comment from Technology Appraisals
Response noted.
A review of TA250 should be planned into the appraisal work programme as an STA. It is proposed to seek a broad remit covering the full licensed indication for eribulin for breast cancer, and carry out an STA that includes the review of TA250 (third- or subsequent-line treatment) together with an appraisal of the extended indication (second-line treatment).
The subgroup eribulin v TPC after capecitabine was not evaluated in TA250. This reflects clinical practice and is a specified subgroup in the EMBRACE trial and containing 559 patients (3/4 of the trial population).

The current indication for eribulin is broad and Eisai will be requesting a restricted position in line with the evidence and clinical practice.

Restriction requested

“Patients with LABC/MBC who have progressive disease after at least two prior chemotherapy regimens for advanced disease which includes capecitabine. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting unless contraindicated.”

3. Quality of life data

QoL was collected from a second phase III trial (study 301) that recruited 1102 patients with advanced metastatic breast cancer (MBC) who had received prior anthracyclines and taxanes using QLQ-C30. This included patients who were treated for first, second and third line MBC. The QLQ-C30 results are converted into EQ-5D utility scores that are used in the economic analysis as QoL was not collected from the EMBRACE trial.

A utility mapping exercise was conducted using a published regression algorithm developed for patients with locally advanced breast cancer to convert the QLQ-C30 questionnaire results into EQ-5D derived utility scores.

| Utility scores of patient on eribulin and TPC |
|-----------------|-----------------|
|                | Eribulin | TPC |
| Baseline       | 0.713     | 0.713 |
| Tumour Response| 0.801     | 0.801 |
| Progression    | 0.695     | 0.695 |

Source: Eribulin 301 clinical trial

NICE appraises health technologies within their marketing authorisation. In its evidence submission to NICE, the company may make a case for a subgroup of the licensed population with adequate justification, and the Committee would consider this (in line with the Guide to the methods of technology appraisal 2013, section 5.10) and make a decision as to whether or not it can be accepted.
4. **Patient access scheme**
   A new patient access scheme has been submitted to the Department of Health

5. **Reduction in drug wastage**
   A new 3ml vial has been launched in the UK in March 2015 (6) that will help to reduce wastage when administering eribulin. Previously eribulin was only available in a 2ml vial preparation. 5mls of eribulin per administration are required when using the average BSA for breast cancer of 1.74m². This can now be achieved using a 2ml and 3ml vial instead of three 2ml vials thus substantially reducing the wastage that was accounted for in TA250.

**Summary**
As is common in cancer treatment, new evidence emerges once a product is launched in a market.

Eisai believes that a review of TA250 is warranted that can take account of the new evidence base: new mature overall survival data, a clearly defined population in keeping with clinical practice, QoL data from patients with advanced breast cancer following anthracycline and taxane treatment, new additional eribulin presentation and the new patient access scheme.

**References**


5. Velikova G, et al. Health-related quality of life (HRQOL) and disease symptoms in patients (pts) with locally advanced or metastatic breast cancer (MBC) treated with eribulin (ERI) or capecitabine (CAP) in a post anthracycline and taxane
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<th>setting. Abstract #6906 and Poster #392P presented at the European Society for Medical Oncology Congress ESMO, Sep 26-Sep 30, 2014</th>
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<td>6. Halaven Summary of Product Characteristics (SPC), June 2014</td>
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**Paper signed off by:** Helen Knight, 16 July 2015

**Contributors to this paper:**

- **Technical Lead:** Ahmed Elsada
- **Project Manager:** Andrew Kenyon