NICE National Institute for Health and Care Excellence

NICE guidance

# Eribulin for treating locally advanced or metastatic breast cancer after 2 or more chemotherapy regimens

Technology appraisal guidance
Published: 21 December 2016

www.nice.org.uk/guidance/ta423

# Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

# Contents

This guidance replaces TA250.

This guidance should be read in conjunction with TA515.

# 1 Recommendations

1.1 Eribulin is recommended as an option for treating locally advanced or metastatic breast cancer in adults, only when:

- it has progressed after at least 2 chemotherapy regimens (which may include an anthracycline or a taxane, and capecitabine)
- the company provides eribulin with the discount agreed in the patient access scheme.

1.2 This guidance is not intended to affect the position of patients whose treatment with eribulin was started within the NHS before this guidance was published. Treatment of those patients may continue without change to whatever funding arrangements were in place for them before this guidance was published until they and their NHS clinician consider it appropriate to stop.

# 2 The technology

## Description of the technology

Eribulin (Halaven, Eisai) is a synthetic analogue of halichondrin B, which inhibits tubulin polymerisation. This disrupts the assembly and formation of microtubules, stopping cancer cell division.

## Marketing authorisation

Eribulin has a UK marketing authorisation for the treatment of adult patients with locally advanced or metastatic breast cancer who have progressed after at least 1 chemotherapeutic regimen for advanced disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting unless these treatments were not suitable.

This appraisal is only looking at locally advanced or metastatic breast cancer that has progressed after 2 or more chemotherapy regimens for advanced disease.

## Adverse reactions

The adverse reactions of eribulin include fatigue, alopecia, peripheral neuropathy, nausea, neutropenia, leukopenia and anaemia. For full details of adverse reactions and contraindications, see the summary of product characteristics.

## Recommended dose and schedule

The recommended dosage of eribulin as the ready to use solution is 1.23 mg/m$^2$ administered intravenously over 2 to 5 minutes on days 1 and 8 of every 21-day cycle.

## Price

The cost of eribulin is £361.00 per 0.88 mg/2 ml solution for injection vial and £541.50 per 1.32 mg/3 ml solution for injection vial (excluding VAT; British national formulary [BNF]

online, accessed September 2016).

The company has agreed a patient access scheme with the Department of Health. This scheme provides a simple discount to the list price of eribulin, with the discount applied at the point of purchase or invoice. The level of the discount is commercial in confidence. The Department of Health considered that this patient access scheme does not constitute an excessive administrative burden on the NHS.

# 3 Evidence

This appraisal is a review of NICE's guidance TA250. The relevant evidence submitted by the company (Eisai) is the data for the subgroup of patients who had locally advanced or metastatic breast cancer that has progressed after 2 or more chemotherapy regimens for advanced disease, which includes capecitabine (if indicated, referred to as subgroup 2 in their submission). The appraisal committee considered this evidence alongside a review of the company submission by the evidence review group (ERG). See the committee papers for full details of the evidence.

# 4 Committee discussion

The appraisal committee reviewed the data available on the clinical and cost effectiveness of eribulin, having considered evidence on the nature of locally advanced or metastatic breast cancer and the value placed on the benefits of eribulin by people with the condition, those who represent them, and clinical experts. It also took into account the effective use of NHS resources.

## Symptoms and management of advanced breast cancer

4.1 The committee heard from a patient expert that locally advanced or metastatic breast cancer is a debilitating condition that can affect women of all ages, and leads to premature death. It also heard that the symptoms of advanced breast cancer can differ substantially among patients, depending on the type of disease and the site of metastases, and the patient expert emphasised that living with advanced breast cancer is very difficult for patients and their families. The life expectancy of people for whom eribulin is licensed is short, and quality of life is very important. For some people even relatively short extensions to life are highly valued, particularly if they are able to experience important events like a child starting school or a family wedding, as long as their quality of life is maintained. The committee heard that having more treatment options available would be very important for patients, giving hope to them and their families. The committee recognised that the availability of additional treatment options for advanced disease would be valued by patients and their families.

4.2 The committee discussed the management of advanced breast cancer with the clinical expert. It heard that the treatment of advanced disease is consistent with NICE's guideline on advanced breast cancer. Initially patients are offered an anthracycline, if they have not had one at an earlier stage in the treatment pathway, or they have a taxane. This is usually followed by capecitabine. The clinical expert estimated that about half of people will then be offered vinorelbine, and overall probably about three quarters of people will be offered either vinorelbine or gemcitabine. The committee was aware that eribulin has a marketing authorisation that covers both the treatment of HER2-positive and

HER2-negative advanced breast cancer. People with HER2-positive disease would initially be treated with targeted therapies, but might benefit from eribulin later in the treatment pathway. The committee noted that eribulin has been available through the Cancer Drugs Fund since 2011 for people with locally advanced or metastatic breast cancer, whose disease has progressed after at least 2 chemotherapy regimens. The committee concluded that eribulin is particularly valuable, and has been more widely used, for HER2-negative disease because this has fewer treatment options.

4.3 The committee considered the most relevant comparators for eribulin in clinical practice. It noted that although the comparators in the scope were defined as vinorelbine, capecitabine or gemcitabine, the comparator in the company submission was treatment of physician's choice (TPC), which was used in the EMBRACE clinical trial. This combined comparator included vinorelbine, gemcitabine, anthracyclines (doxorubicin) and taxanes (paclitaxel and docetaxel). The committee heard from the clinical expert that this reflects UK clinical practice because it includes all available options for this patient population, and most people would already have had capecitabine. The committee therefore concluded that TPC is a reasonable proxy for usual care in the NHS and a clinically relevant comparator for the population under consideration in this appraisal. It did however note that the majority of people (three quarters) would be offered vinorelbine or gemcitabine as an alternative to eribulin at this stage in the treatment pathway.

# Clinical effectiveness

4.4 The committee considered the clinical evidence for eribulin compared with TPC from the EMBRACE trial. This was a randomised controlled trial in women with locally advanced or metastatic breast cancer, who had had 2 to 5 chemotherapy regimens for advanced disease. The committee noted that the company presented data for the whole trial population and for a subgroup of people who previously had capecitabine, because they considered this population to be the most relevant to clinical practice in the UK. The committee agreed that the subgroup who had had capecitabine, from the company submission, was the most clinically relevant population and noted that approximately 80% of people having eribulin through the Cancer Drugs Fund had previously had capecitabine.

It heard from the clinical expert that the design of EMBRACE reflects current clinical practice, and that the results are consistent with subsequent real-life use of eribulin through the Cancer Drugs Fund. The committee noted that the primary outcome of the trial was overall survival. At the submission 95% of the population in the subgroup had died and there was a 2.9 month difference in median overall survival favouring eribulin, which was statistically significant. The committee concluded that the results of EMBRACE are generalisable to the UK population, and agreed that the subgroup of people who had prior capecitabine is the most relevant population for this appraisal. It also concluded that based on the available evidence, eribulin is clinically effective and offers a statistically significant improvement in overall survival compared with TPC.

4.5 Health-related quality-of-life data were not collected in EMBRACE, therefore the company presented results from another clinical trial for eribulin compared with capecitabine (Study 301). The committee noted that the population in Study 301 was less heavily pre-treated (had no more than 2 chemotherapy regimens, compared with 2 to 5 in EMBRACE) and had not previously had capecitabine. The committee also understood that the number of people completing the health-related quality-of-life questionnaire declined towards the end of the study period, and that data for 24 months is only available from 13 people in the eribulin arm. However it considered that this is a general problem in clinical trials, and welcomed the fact that there was data available directly from patients who had taken eribulin. The committee concluded that direct patient data on health-related quality of life from Study 301 is of value, but has inherent limitations.

# Cost effectiveness

4.6 The committee considered the cost-effectiveness evidence presented by the company and its critique by the ERG. It accepted the structure of the economic model developed by the company and went on to discuss some of the key assumptions within the model.

## Utility values

4.7 The committee noted that the company used a mapping algorithm published by

Crott and Briggs (2010) for estimating utility values from the health-related quality-of-life data from Study 301. It heard from the ERG that this algorithm was developed using data from people with locally advanced but not metastatic breast cancer and who had good baseline health status. The ERG also noted that this resulted in only a small decrease in the utility between the progression-free and post-progression health states in the company's model (approximately 3%), which it considered to be implausible. The ERG used the utility values from a study by Lloyd et al. (2006), which it considered to be more relevant. The study assessed UK-based societal preferences for different stages of metastatic breast cancer, and has been used in other NICE appraisals. This resulted in an approximate 20% decline in utility between the pre- and post-progression state, and an increase in the incremental cost-effectiveness ratio (ICER) of around £11,000 per QALY gained. The committee heard from the clinical expert that patients may have radiological evidence of disease progression without any immediate deterioration in symptoms or quality of life, although this would be expected to decline as the disease progressed further. The clinical expert said that some decline would be expected, but that an immediate decrease of 20% in health-related quality of life on progression seemed high. The committee considered that the very small decrement seen in the company's model, although generated directly from an eribulin trial, may be an underestimate. However, the estimate of 20% deterioration in quality of life on progression from the Lloyd et al. study also has limitations. The committee could not confidently determine whether the Lloyd et al. estimate was more or less accurate than that which resulted from the company's mapping. It concluded that the most plausible utility value for the progressed disease health state is likely to be somewhere between the company's and the ERG's estimates.

# Treatment costs

## Calculating body surface area

4.8 The committee noted that the dose of eribulin and its comparators are dependent on body surface area. It heard from the ERG that the company calculated doses using the standard error instead of the standard deviation of the population, which is methodologically implausible, and resulted in a narrow range of body surface areas and drug dosages in the company model. The ERG changed this in

its revised base case. The change in individual doses had little impact on cost of the drugs administered but increased the drug wastage, calculated from unused portions of vials, leading to an increase in total drug costs, especially of eribulin. The committee acknowledged that drug wastage is an issue when doses are individually calculated according to weight or body surface area and noted that some drug wastage had already been included in the company's base case (when the company excluded wastage in a sensitivity analysis the ICER decreased by 55%). The committee heard from the company that data on individual patient doses used in EMBRACE are not available. The committee heard from the clinical expert that in clinical practice drug wastage is recognised and efforts are made to minimise it by carefully scheduling patients for treatment where vial sharing is possible, although the proportion of drug cost saved through vial sharing in clinical practice is uncertain. The committee agreed that drug wastage may be higher than in the company's model, but that the ERG estimate is likely to be a conservative scenario.

## Subsequent line of therapy

4.9 The committee noted that the company applied a 6-month cap on the total treatments a patient could have in the model. The committee heard from the company that this was based on data on the proportion of breast cancer patients progressing from first to fifth-line therapy (Kantar Health, 2014) and is consistent with the results from EMBRACE, in which the majority of people had 3 to 6 cycles of eribulin. It heard from the ERG that a cap for all lines of treatment is implausible and likely to result in an underestimate of the costs of subsequent therapy. The ERG assumed that after progression 60% of patients would go on to have subsequent therapy until death, based on data on the proportion of breast cancer patients progressing from first to fifth-line therapy (Kantar Health, 2014). The committee heard from the clinical expert that the response to third-line treatment is variable; some people have chemotherapy sensitive disease and may continue on eribulin beyond 6 months, and these people may also respond well to subsequent lines of treatment. Others have disease that progresses quickly on eribulin, probably because they have chemotherapy insensitive disease, and these patients may decide not to have further treatments. The committee agreed with the ERG's reasoning on continuing treatment beyond 6 months, although it considered that there is significant uncertainty about the proportion of patients

who might still be on treatment after 6 months, and the duration of subsequent lines of treatment. The committee acknowledged that the subsequent treatments are a source of significant uncertainty in the model, which it is not possible to resolve. It therefore concluded that although the assumptions in the company's model might have been optimistic, the ERG's assumption represents a worst-case scenario for the costs of subsequent therapy.

### Cost of comparators

4.10 The committee considered the sensitivity analysis presented by the company, which showed that if the percentage of people taking the comparators were changed to 50% gemcitabine and 50% vinorelbine, the ICER decreased substantially (by approximately 33%). It was mindful of its previous conclusion that most people would be offered vinorelbine or gemcitabine after 2 or more chemotherapy regimens (see section 4.2). It also noted that in EMBRACE only 65% of patients had these 2 agents and that assuming that 75% of patients would have gemcitabine or vinorelbine would reduce the ICER in favour of eribulin.

## Additional changes to the model by the ERG

4.11 The committee considered the additional changes to the model, which included updating the progression-free survival and overall survival data, applying annual discounting, and correcting errors in the cost calculations. The committee noted that these were not cost drivers and did not have a major impact on the cost-effectiveness results. It accepted that these were methodological corrections and concluded that they were appropriate.

## Cost-effectiveness results

4.12 The committee considered the most plausible ICER for eribulin compared with TPC. It was mindful of its previous considerations on the different assumptions and inputs to the model and concluded that the most plausible ICER for eribulin compared with TPC is likely to be between the company's base case ICER (£35,624 per quality-adjusted life year [QALY] gained) and the ERG's revised

base case (£62,672 per QALY gained). It also considered that there were a lot of uncertainties around the assumptions in the model, many of which could not be resolved. The committee noted that although it is not possible to determine a precise ICER for eribulin compared with TPC, some of the ERG's assumptions were based on highly conservative scenarios. The committee also noted that if the costs of TPC were increased (to account for a higher use of gemcitabine and vinorelbine in clinical practice than that in the model) this would further reduce the ICER for eribulin compared with TPC.

# Innovation

4.13 The committee heard from the company that it considers eribulin to be innovative because of its mechanism of action and convenient administration method (it is administered intravenously over 2 to 5 minutes with no special handling or tubing needed). The committee heard from the patient and clinical expert that a quick and easily administered preparation would enable appointments to be scheduled around normal daily life and activities (for example, work and carer commitments). However, the committee concluded that it could not identify any specific health-related benefit that had not already been captured in the QALY calculation.

# End-of-life considerations

4.14 The committee considered the advice about life-extending treatments for people with a short life expectancy in NICE's final Cancer Drugs Fund technology appraisal process and methods. It considered that the evidence presented by the company showed that people with advanced breast cancer that has progressed after 2 lines of chemotherapy have a life expectancy of less than 24 months. The overall survival of people in EMBRACE was a mean of 13.53 months in the TPC arm. The committee also considered that both the company's and the ERG's models suggest that eribulin offers a mean overall survival benefit of more than 3 months. In light of the short life expectancy at this stage of breast cancer, the committee considered this overall survival benefit to be substantial. The committee therefore concluded that eribulin met the end-of-life criteria

objectively and robustly and that it can be considered a life-extending, end-of-life treatment.

# Pharmaceutical Price Regulation Scheme (PPRS) 2014

4.15 The committee was aware of NICE's position statement on the Pharmaceutical Price Regulation Scheme (PPRS) 2014, and in particular the PPRS payment mechanism. It accepted the conclusion 'that the 2014 PPRS payment mechanism should not, as a matter of course, be regarded as a relevant consideration in its assessment of the cost effectiveness of branded medicines'. The committee heard nothing to suggest that there is any basis for taking a different view about the relevance of the PPRS to this appraisal. It therefore concluded that the PPRS payment mechanism was not relevant in considering the cost effectiveness of the technology in this appraisal.

# Conclusions

4.16 The committee concluded that the correct modelling approach is uncertain but it found no evidence to indicate that the ERG's approach was based on more plausible assumptions than the company's approach. It noted that although it is not possible to determine a precise ICER for eribulin compared with TPC, some of the ERG's assumptions were based on highly conservative scenarios. The committee considered the most plausible ICER would be much lower than that calculated by the ERG, and was likely to be below £50,000 per QALY gained (see section 4.12). However it considered that if the percentage of people taking vinorelbine and gemcitabine in the TPC arm were increased, in line with UK clinical practice (see section 4.2), the ICER would be further reduced. It was satisfied that the ICER for eribulin was acceptable given the additional weight that can be assigned to QALY gains for a treatment that fulfils the end-of-life criteria.

# Summary of appraisal committee's key conclusions

## Key conclusion

Eribulin is recommended as an option for treating locally advanced or metastatic breast cancer in adults, only when:

- it has progressed after at least 2 chemotherapy regimens (which may include an anthracycline or a taxane and capecitabine)
- the company provides eribulin with the discount agreed in the patient access scheme.

The committee concluded that the correct modelling approach is uncertain but it found no evidence to indicate that the evidence review group (ERG's) approach was based on more plausible assumptions than the company's approach.

The most plausible incremental cost-effectiveness ratio (ICER) for eribulin compared with treatment of physician's choice (TPC) is likely to be between the company's base case ICER (£35,624 per quality-adjusted life year [QALY] gained) and the ERG's revised base case (£62,672 per QALY gained). Although it is not possible to determine a precise ICER for eribulin compared with TPC, some of the ERG's assumptions were based on highly conservative scenarios. The committee considered the most plausible ICER would be much lower than that calculated by the ERG, and was likely to be below £50,000 per QALY gained. However it considered that if the percentage of people taking vinorelbine and gemcitabine in the TPC arm were increased, in line with UK clinical practice, the ICER would be further reduced. It was satisfied that the ICER for eribulin was acceptable given the additional weight that can be assigned to QALY gains for a treatment that fulfils the end of life criteria.

See sections 1.1, 4.12 and 4.16

## Current practice

### Clinical need of patients, including the availability of alternative treatments

The majority of people (three quarters) would be offered vinorelbine or gemcitabine as an alternative to eribulin after 2 or more chemotherapy regimens. Eribulin has been available through the Cancer Drugs Fund since 2011 for people with locally advanced or metastatic

breast cancer, whose disease has progressed after at least 2 chemotherapy regimens. The committee concluded that eribulin is particularly valuable, and has been more widely used, for HER2-negative disease because this has fewer treatment options. It also recognised that the availability of additional treatment options for advanced disease would be valued by patients and their families.

See sections 4.1 to 4.3

## The technology

### Proposed benefits of the technology: how innovative is the technology in its potential to make a significant and substantial impact on health-related benefits?

Eribulin was associated with a statistically significant overall survival gain of 2.9 months, compared with TPC in the EMBRACE trial. The committee concluded that the results of EMBRACE are generalisable to the UK population, and agreed that the subgroup of people who had had capecitabine is the most relevant population for this appraisal. It also concluded that eribulin is clinically effective.

The committee heard from the company that it considers eribulin to be innovative because of its mechanism of action and convenient administration method. However, it concluded that it could not identify any specific health-related benefit that had not already been captured in the QALY calculation.

See sections 4.4 and 4.13

### What is the position of the treatment in the pathway of care for the condition?

Initially patients with locally advanced or metastatic breast cancer are offered an anthracycline, if they have not had one at an earlier stage in the treatment pathway, or they have a taxane. This is usually followed by capecitabine. The clinical expert estimated that about half of people will then be offered vinorelbine, and overall about three quarters of people will be offered either vinorelbine or gemcitabine, as an alternative to eribulin.

See section 4.2

### Adverse reactions

The adverse reactions of eribulin include fatigue, alopecia, peripheral neuropathy, nausea, neutropenia, leukopenia and anaemia. For full details of adverse reactions and contraindications, see the summary of product characteristics.

See section 2

## Evidence for clinical effectiveness

### Availability, nature and quality of evidence

The clinical evidence for eribulin compared with TPC comes from the EMBRACE trial. The committee noted that the company presented data for the whole trial population and for a subgroup of people who previously had capecitabine, because they considered this population to be the most relevant to clinical practice in the UK. The committee agreed that the subgroup who had had capecitabine, from the company submission, was the most clinically relevant population and noted that approximately 80% of people having eribulin through the Cancer Drugs Fund had previously had capecitabine.

Health-related quality-of-life data was not collected in EMBRACE, therefore the company presented results from another clinical trial for eribulin compared with capecitabine (Study 301). The population in the study was less heavily pre-treated and had not previously had capecitabine.

See sections 4.4 and 4.5

### Relevance to general clinical practice in the NHS

The committee concluded that the results of EMBRACE are generalisable to the UK population, and agreed that the subgroup of people who had had capecitabine is the most relevant population for this appraisal. It also concluded that TPC is a reasonable proxy for usual care in the NHS and a clinically relevant comparator for the population under consideration in this appraisal. It did however note that the majority of people (three quarters) would be offered vinorelbine or gemcitabine as an alternative to eribulin at this stage in the treatment pathway.

See sections 4.2 and 4.4

### Uncertainties generated by the evidence

Health-related quality-of-life data was not collected in EMBRACE, therefore the company presented results from another clinical trial for eribulin compared with capecitabine (Study 301). The population in Study 301 was less heavily pre-treated and had not previously had capecitabine. The committee considered that direct patient data on health-related quality of life is of value, but it has limitations.

See section 4.5

### Are there any clinically relevant subgroups for which there is evidence of differential effectiveness?

The committee agreed that the subgroup of people who had had capecitabine is the most relevant population for this appraisal.

See section 4.4

### Estimate of the size of the clinical effectiveness including strength of supporting evidence

Eribulin was associated with a statistically significant overall survival benefit of 2.9 months when compared with TPC.

See section 4.4

### For reviews: How has the new clinical evidence that has emerged since the original appraisal (TA250) influenced the current recommendations?

At the time of the appraisal for NICE's guidance TA250, evidence was available from a data-cut when 77% of patients in the trial had died. At the time of the submission for the current appraisal, 95% of the trial population had died and therefore more mature data was available.

Health-related quality-of-life data was not collected in EMBRACE and in TA250 the company presented results from 2 phase 2, multi-centre, single-arm, open-label trials (Study 201 and Study 211). At the time of the current appraisal results from a phase 3, open label randomised controlled trial for eribulin compared with capecitabine had

become available (Study 301).

See sections 4.4 and 4.5

## Evidence for cost effectiveness

### Availability and nature of evidence

The committee accepted the structure of the economic model developed by the company and considered its critique by the ERG.

See section 4.6

### Uncertainties around and plausibility of assumptions and inputs in the economic model

The committee considered the following key areas of uncertainty:

- utility values used in the model for the progressed disease health state, in both arms of the model
- the method used for calculating body surface area and dose of eribulin and its comparators
- the method used for calculating the costs of subsequent line of therapy the method used for calculating the costs of comparators.

See sections 4.7 to 4.10

### Incorporation of health-related quality-of-life benefits and utility values: have any potential significant and substantial health-related benefits been identified that were not included in the economic model, and how have they been considered?

The company used a mapping algorithm published by Crott and Briggs (2010) for estimating utility values from the health-related quality-of-life data from Study 301. This resulted in only a small decrease in the utility between the progression-free and post-progression health states in the company's model (approximately 3%). The ERG

considered this to be implausible and used utility values from a study by Lloyd at al. (2006), This resulted in an approximate 20% decline in utility between the pre- and post-progression state and increase in the ICER of around £11,000 per QALY gained.

The committee considered that the very small decrement seen in the company's model, although generated directly from an eribulin trial, may be an underestimate but the 20% deterioration in quality of life on progression seemed to be too high. It concluded that the most plausible utility value for the progressed disease health state is likely to be somewhere between the company's and the ERG's estimates.

The committee heard from the company that it considers eribulin to be innovative because of its mechanism of action and convenient administration method. However, it concluded that it could not identify any specific health-related benefit that had not already been captured in the QALY calculation.

See sections 4.7 and 4.14

### Are there specific groups of people for whom the technology is particularly cost effective?

The committee considered that the subgroup of people who had had capecitabine is the most relevant population for this appraisal.

See section 4.4

### What are the key drivers of cost effectiveness?

The key drivers of cost effectiveness in the company's model were the utility value used in the progressed disease heath state in both arms of the model and the price of eribulin.

### Most likely cost-effectiveness estimate (given as an ICER)

The committee concluded that the most plausible ICER for eribulin compared with TPC is likely to be between the company's base case ICER (£35,624 per QALY gained) and the ERG's revised base case (£62,672 per QALY gained). There were a lot of uncertainties around the assumptions in the model, therefore it was not possible to determine a precise ICER. The committee considered the most plausible ICER to be below £50,000 per QALY gained. The committee noted that if the costs of TPC were increased (to account for a

higher use of gemcitabine and vinorelbine in clinical practice than that in the model) this would further reduce the ICER for eribulin compared with TPC.

See sections 4.12 and 4.16

### For reviews: How has the new cost-effectiveness evidence that has emerged since the original appraisal (TA250) influenced the current recommendations?

Eribulin was not recommended in NICE's guidance TA250 for the treatment of locally advanced or metastatic breast cancer that has progressed after at least 2 chemotherapy regimens for advanced disease, because the most plausible ICER was much higher than the range normally considered a cost-effective use of NHS resources, even taking into account additional weights applied to QALY benefits for a life-extending treatment at the end of life.

Updated survival results from the EMBRACE trial were incorporated in the current appraisal and also results for health-related quality-of-life from a phase 3, open label randomised controlled trial for eribulin compared with capecitabine (Study 301).

The committee concluded that the correct modelling approach was uncertain and therefore the most plausible ICER for eribulin compared with TPC is likely to be between the company's base case ICER and the ERG's revised base case. There were a lot of uncertainties around the assumptions in the model, therefore it was not possible to determine a precise ICER. The committee considered the most plausible ICER to be below £50,000 per QALY gained. However it considered that if the percentage of people taking vinorelbine and gemcitabine in the TPC arm were increased, in line with UK clinical practice, the ICER would be further reduced. Therefore it was satisfied that the most plausible ICER was acceptable given the additional weight that can be assigned to QALY gains, for a treatment that fulfils the end-of-life criteria.

See sections 4.12 and 4.16

## Additional factors taken into account

### Patient access schemes (PPRS)

The PPRS payment mechanism was not relevant in considering the cost effectiveness of the technology in this appraisal.

See section 4.15

## End-of-life considerations

The evidence shows that people with advanced breast cancer that has progressed after 2 lines of chemotherapy have a life expectancy of less than 24 months.

The evidence also suggests that eribulin offers a mean overall survival benefit of more than 3 months. In light of the short life expectancy at this stage of breast cancer, the committee considered this overall survival benefit to be substantial.

The committee concluded that eribulin met the end-of-life criteria objectively and robustly and that it can be considered a life-extending, end-of-life treatment.

See section 4.14

## Equalities considerations and social value judgements

No equality issues were raised during the appraisal.

# 5 Implementation

5.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires clinical commissioning groups, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.

5.2 The Welsh Assembly Minister for Health and Social Services has issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 3 months of the guidance being published.

5.3 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has locally advanced or metastatic breast cancer and the doctor responsible for their care thinks that eribulin is the right treatment, it should be available for use, in line with NICE's recommendations.

# 6 Appraisal committee members and NICE project team

## Appraisal committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee A.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each appraisal committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

## NICE project team

Each technology appraisal is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

**Boglarka Mikudina**
Technical Lead

**Eleanor Donegan**
Technical Adviser

**Liv Gualda**
Project Manager

ISBN: 978-1-4731-2230-7