National Institute for Health and Clinical Excellence

Health Technology Appraisal

Ixabepilone for locally advanced or metastatic breast cancer

Response to consultee and commentator comments on the draft scope

Comment 1: the draft remit

Section	Consultees	Comments	Action
Appropriateness	Breakthrough Breast Cancer	Ixabepilone may provide an addition to the armoury of therapies available for women with advanced breast cancer, particularly where the breast cancer is resistant to other chemotherapies. Patients with locally advanced or metastatic breast cancer typically have limited treatment options and those with resistant tumours will have further limitations as to their options. There needs to be a range of treatments available as not all will be suitable to individual patient needs. Furthermore, patients with locally advanced or metastatic breast cancer, understandably, want access to treatments that will give them the chance of both an increased length of survival and improved quality of life to spend more quality time with their friends and families. For women with locally advanced or metastatic breast cancer, the importance of quality of life cannot be underestimated.	Comment noted
	Breast Cancer Care	Breast Cancer Care believes it would be appropriate to refer the topic of Ixabepilone for locally advanced or metastatic breast cancer to NICE for appraisal. Ixabepilone could offer a further treatment option for people who have become resistant to the usual regime of available chemotherapy. In particular it would offer a further option for people with triple negative breast cancer for whom there are less treatment options.	Comment noted
	National Collaborating Centre for Cancer	Yes, a novel agent with apparent activity in breast cancer.	Comment noted
	Bristol Myers Squibb Pharmaceuticals	Ixabepilone is an appropriate topic to refer to NICE.	Comment noted

Section	Consultees	Comments	Action
	Roche	The appraisal should not be started until there is clarity around the precise licensing timelines and the wording of the indications (monotherapy and combination therapy) is finalised with the EMEA.	In planning the production of timely guidance the Institute takes into account estimated timings of marketing authorisation. Ixabepilone will be appraised within its marketing authorisation
Wording	Breakthrough Breast Cancer	We believe the wording of the remit reflects the issues of clinical and cost effectiveness about this technology that NICE should consider. It should be noted that this scope is being drawn up on assumptions as to what the licensed indication will be, as Ixabepilone is not yet licensed.	Comment noted
	Breast Cancer Care	We believe the wording of the remit reflects the issues of clinical and cost effectiveness about this technology that NICE should consider.	Comment noted
	National Collaborating Centre for Cancer	yes	Comment noted
	Bristol Myers Squibb Pharmaceuticals	The wording of the remit is appropriate to this appraisal.	Comment noted

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	Roche	The remit does not explicitly define the patient population for which this treatment is indicated or following which line of treatment. The remit needs to be clearer in terms of which advanced or metastatic breast cancer patients are eligible to be treated with ixabepilone, either alone or in combination with capecitabine. It should be aligned with the description under the section entitled Population "women with advanced or metastatic breast cancer where previous chemotherapy has included anthracycline, taxanes and capecitabine." It should also stipulate wheather these treatments should have been received in the metastatic setting, as per the registration trial. The wording also needs to be reflective of the licence wording.	Ixabepilone will be appraised within its market authorisation
Timing Issues	Breakthrough Breast Cancer	Patients with locally advanced or metastatic breast cancer typically have limited treatment options and those with resistant tumours will have further limitations as to their options. Time is of the greatest importance to people with metastatic breast cancer for whom it is limited, therefore we would welcome a prompt appraisal of this treatment so that it may reach those who may benefit quickly, if recommended by NICE.	Comment noted
	Breast Cancer Care	Breast Cancer Care believes that this proposed appraisal is urgent. As metastatic breast cancer is not curable it is essential that effective treatment options which could delay progression or improve survival are made available to this patient group as quickly as possible.	Comment noted
	National Collaborating Centre for Cancer	Appropriate with 15th wave	Comment noted
	Bristol Myers Squibb Pharmaceuticals	As Ixabepilone is not yet licensed, timing of this appraisal should reflect the licensing timelines. In addition, BMS are expecting results of a pivotal trial to become available in [redacted]. As these results will be important in informing the submission, this timing should be taken into account in the scheduling process.	Comment noted

Section	Consultees	Comments	Action
	Roche	The appraisal should not be started until there is clarity around the precise licensing timelines and the wording of the indication is finalised by the EMEA.	In planning the production of timely guidance the Institute takes into account estimated timings of marketing authorisation. Ixabepilone will be appraised within its marketing authorisation

Comment 2: the draft scope

Section	Consultees	Comments	Action
Background information	Breakthrough Breast Cancer	The background information appears to adequately reflect the situation as regards breast cancer. However, we would welcome the inclusion of information as to what it means to the patient to have locally advanced or metastatic breast cancer – e.g. the impact upon their quality of life.	Comment noted. The background section is intended as a brief summary of background information. Consultees are now invited to submit statements in line with the Guide to the STA process, http://www.nice.org.uk/media/8DE/74/STA_Process_Guide.pdf, and these may include more comprehensive information.
	Breast Cancer Care	The background information is accurate.	Comment noted
	National Collaborating Centre for Cancer	General emphasis is satisfactory. I would disagree with the figures in the third paragraph where it is stated that 20% present with advanced or metastatic disease and 40-50% of the remainder eventually develop metastatic disease. This would leave slightly less than 50% of the overall 'breast cancer population' with a recurrence-free situation. It would generally be considered as higher than that currently, these would appear to be old figures. At the start of paragraph 4 of this section metastatic disease and advanced disease are bracketed together. Given current adjuvant management of advanced disease (using the definition in the background section) the aim of treatment is permanent disease-free survival, not the lesser aims stated.	Comments noted. The background section is intended as a brief summary of background information. Consultees are now invited to submit statements in line with the Guide to the STA process, http://www.nice.org.uk/media/8DE/74/STA_Process_Guide.pdf, and more comprehensive up to date information in these statements is welcomed. The scope has not been amended on this occasion as updated information was not brought to light.

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	Bristol Myers Squibb Pharmaceuticals	The background information is appropriate for the purposes of the scope document.	Comment noted
	Roche	No comment	Comment noted
The technology/ intervention	Breakthrough Breast Cancer	The description of the technology is accurate.	Comment noted
	Breast Cancer Care	The description of the technology is accurate.	Comment noted
	National Collaborating Centre for Cancer	yes	Comment noted
	Bristol Myers Squibb Pharmaceuticals	The description of Ixabepilone is accurate.	Comment noted
	Roche	No comment	Comment noted
Population	Breakthrough Breast Cancer	The population is appropriately defined.	Comment noted
	Breast Cancer Care	The population definition appears to be accurate.	Comment noted
	National Collaborating Centre for Cancer	yes	Comment noted
	Bristol Myers Squibb Pharmaceuticals	The population to be considered by the appraisal appropriately represents the trials and patient group.	Comment noted

Section	Consultees	Comments	Action
	Roche	It should be stipulated that the previous therapies of “anthracycline, taxanes and capecitabine” should have been administered in the metastatic setting, as in the clinical trial.	Comment noted, ixabepilone will be appraised within its marketing authorisation and in line the with updated Guide the Methods of Technology Appraisal: http://www.nice.org.uk/media/B52/A7/TAMethodsGuideUpdatedJune2008.pdf
Comparators	Breakthrough Breast Cancer	In principle, we agree that comparison with appropriate chemotherapy regimens in standard practice would be suitable. However, comparator options may be limited. Standard regimens often include anthracyclines and taxanes and the population to be assessed in this appraisal are those who may have previously failed to respond to such treatments. Comparisons with these chemotherapies may therefore be inappropriate.	Comment noted. Following consultation and the scoping workshop, the comparators in the scope are defined as: capecitabine, vinorelbine and taxane containing regimens and other appropriate chemotherapy regimens in standard practice in England and Wales. Ixabepilone will be appraised in line with the Guide the Methods of Technology Appraisal: http://www.nice.org.uk/media/B52/A7/TAMethodsGuideUpdatedJune2008.pdf.

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	Breast Cancer Care	No specific regimens have been named but the definition would cover a range of relevant chemotherapy regimens. Vinorelbine and gemcitabine would be appropriate comparators.	Comment noted. Following consultation and the scoping workshop, the comparators in the scope are defined as: capecitabine, vinorelbine and taxane containing regimens and other appropriate chemotherapy regimens in standard practice in England and Wales. Ixabepilone will be appraised in line with the Guide the Methods of Technology Appraisal: http://www.nice.org.uk/media/B52/A7/TAMethodsGuideUpdatedJune2008.pdf.
	National Collaborating Centre for Cancer	Where previous therapy includes taxane, anthracycline and Capecitabine then vinorelbine is an appropriate comparator. The combination of Ixabepilone plus capacitabine is appropriate because no activity would expected from re-challenge with Capecitabine alone after Capecitabine failure. For those patients having received prior taxane and anthracycline then Ixabepilone plus Capecitabine is appropriate with the comparators being Capecitabine and vinorelbine either as monotherapy or a combination.	Comment noted. Following consultation and the scoping workshop, the comparators in the scope are defined as: capecitabine, vinorelbine and taxane containing regimens and other appropriate chemotherapy regimens in standard practice in England and Wales. Ixabepilone will be appraised in line with the Guide the Methods of Technology Appraisal: http://www.nice.org.uk/media/B52/A7/TAMethodsGuideUpdatedJune2008.pdf.

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	Bristol Myers Squibb Pharmaceuticals	Potential comparators for this appraisal should include: - Capecitabine. It is the comparator in the pivotal Ixabepilone trials and the commonly used treatment in the UK in the relevant patient population Taxotere. There is evidence showing that patients previously treated with taxotere (the most commonly used taxane in this patient population in the UK), are often re-challenged with taxotere or a taxotere-containing combination therapy	Comment noted. Following consultation and the scoping workshop, the comparators in the scope are defined as: capecitabine, vinorelbine and taxane containing regimens and other appropriate chemotherapy regimens in standard practice in England and Wales. Ixabepilone will be appraised in line with the Guide the Methods of Technology Appraisal: http://www.nice.org.uk/media/B52/A7/TAMethodsGuideUpdatedJune2008.pdf.
	Roche	The chemotherapy regimens in standard practice in England and Wales should be listed. They should include: capecitabine, vinorelbine, capecitabine and taxotere combination, capecitabine and vinorelbine combination, gemcitabine and paclitaxel combination.	Comment noted. Following consultation and the scoping workshop, the comparators in the scope are defined as: capecitabine, vinorelbine and taxane containing regimens and other appropriate chemotherapy regimens in standard practice in England and Wales. Ixabepilone will be appraised in line with the Guide the Methods of Technology Appraisal: http://www.nice.org.uk/media/B52/A7/TAMethodsGuideUpdatedJune2008.pdf.

Section	Consultees	Comments	Action
Outcomes	Breakthrough Breast Cancer	It is important that quality of life is taken into full account in this population group.	Comment noted. Health-related quality of life is listed as an outcome in the scope and will be considered in line with the Guide the Methods of Technology Appraisal: http://www.nice.org.uk/media/B52/A7/TAMethodsGuideUpdatedJune2008.pdf. See section 5.4.
	Breast Cancer Care	Breast Cancer Care believes that progression free survival can be very important psychologically to metastatic patients, who may be very anxious about treatments failing. In terms of health related quailty of life, it is essential that the psychological benefits of treatment are also considered in terms of giving patients hope of increased survival.	Comment noted. Health-related quality of life is listed as an outcome in the scope and will be considered in line with the Guide the Methods of Technology Appraisal: http://www.nice.org.uk/media/B52/A7/TAMethodsGuideUpdatedJune2008.pdf. See section 5.4.
	National Collaborating Centre for Cancer	yes	Comment noted
	Bristol Myers Squibb Pharmaceuticals	The outcomes would capture the most important health related benefits.	Comment noted
	Roche	No comment	Comment noted

Section	Consultees	Comments	Action
Economic analysis	Breakthrough Breast Cancer	We would stress that the importance of quality of life cannot be underestimated for people with locally advanced or metastatic breast cancer and we believe that this should be a significant factor in the analysis of cost-effectiveness.	Comment noted. Health-related quality of life is listed in the scope and will be considered in line with the Guide the Methods of Technology Appraisal: http://www.nice.org.uk/media/B52/A7/TAMethodsGuideUpdatedJune2008.pdf. See section 5.4.
	National Collaborating Centre for Cancer	Appropriate as stated	Comment noted
	Bristol Myers Squibb Pharmaceuticals	The analysis should be conducted in line with the NICE Reference case.	Comment noted. Please note that the Guide to Methods of Technology Appraisal has been updated: http://www.nice.org.uk/media/B52/A7/TAMethodsGuideUpdatedJune2008.pdf
	Roche	The appropriate time horizon for this model would be a life-time time horizon. Therefore, the model will need to capture the life time benefits of the treatments and the associated costs.	Comment noted. Please note that the Guide to Methods of Technology Appraisal has been updated: http://www.nice.org.uk/media/B52/A7/TAMethodsGuideUpdatedJune2008.pdf
Other considerations	Breakthrough Breast Cancer	No comments	Comment noted
	National Collaborating Centre for Cancer	none	Comment noted

Section	Consultees	Comments	Action
	Bristol Myers Squibb Pharmaceuticals	To be discussed at the scoping meeting.	Comment noted
	Roche	What is the likely licence wording?	Ixabepilone does not currently hold a marketing authorisation but it will be appraised within its licensed indications.
Questions for consultation	Breakthrough Breast Cancer	We believe that Ixabepilone should be appraised through the Single Technology Appraisal process. This technology represents another treatment option for this group of patients for whom such options are limited.	Comment noted
	National Collaborating Centre for Cancer	The identification of sub-groups of patients appropriate for this intervention may particularly wish to focus on the group who are resistant or have rapid failure with currently available regimens. Accordance with marketing authorisation is appropriate unless a major omission is identified based on the evidence available.	Comment noted. Consultees agreed at the scoping workshop that this will depend on the availability of evidence.
	Bristol Myers Squibb Pharmaceuticals	This appraisal is considered suitable for the single technology appraisal (STA) process. Given the scale of the STA, a number of potential comparators should be limited in the scope of the appraisal.	Comment noted. This topic has been referred under the Single Technology Appraisal Process, and will be appraised in line the relevant Process and Methods Guides: http://www.nice.org.uk/media/8DE/74/STA_Process_Guide.pdf and http://www.nice.org.uk/media/B52/A7/TAMethodsGuideUpdatedJune2008.pdf.

Section	Consultees	Comments	Action
	Roche	It should be clarified whether the 15% of HER2 positive patients included in the clinical trial were considered refractory or contraindicated to trastuzumab.	Comment noted. Consultees agreed at the scoping workshop that this will depend on the evidence base which will be appraised in line with Guide to Methods of Technology Appraisal has been updated: http://www.nice.org.uk/media/B52/A7/TAMethodsGuideUpdatedJune2008.pdf
Additional comments on the draft scope.	Breakthrough Breast Cancer	No comments	Comment noted

Comment 4: Regulatory issues

Section	Consultees	Comments	Action
Remit	Bristol Myers Squibb Pharmaceuticals	The remit reflects the proposed marketing authorization.	Comment noted

Section	Consultees	Comments	Action
Current or proposed marketing authorisation	Bristol Myers Squibb Pharmaceuticals	Commercial in confidence: [redacted] Currently, the target date for regulatory submission is [redacted] [redacted]	Comment noted

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope

Department of health
Macmillan Cancer Support
GlaxoSmithKline
Kyowa Hakko UK
Marie Curie Cancer Care
Royal Pharmaceutical Society
Eli Lilly
Royal College of nursing
Royal College of pathologists