National Institute for Health and Clinical Excellence

Single Technology Appraisal (STA)

Bevacizumab in combination with non-taxanes for the first-line treatment of metastatic breast cancer

Response to consultee and commentator comments on the draft scope (pre-referral)

Comment: the draft scope

Section	Consultees	Comments	Action
Background information	**Breakthrough Breast Cancer**	The background information is largely accurate however, there are several points which should be amended. The statistics used should be updated to read that 'There were over 40,000 women and **around 250 men** newly diagnosed with breast cancer in England and Wales during **2007**. Furthermore, there were around 12,000 deaths due to breast cancer in the UK in **2008**; an average rate of 38.6 deaths per 100,000 females and **0.2 deaths** per 100,000 males.' This information is found on the Cancer Research UK website at CancerStats, Breast Cancer	Comment noted. Scope amended accordingly.
	Breast Cancer Care	This information appears relevant.	Comment noted. No action required.
The technology/ intervention	**Breakthrough Breast Cancer**	The description of the technology appears to be accurate.	Comment noted. No action required.
	Breast Cancer Care	The description of the use of bevacizumab and non- taxanes appears accurate based on the available research.	Comment noted. No action required.

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Population	**Breakthrough Breast Cancer**	The population appears to be appropriately defined. The mode of action for bevacizumab, unlike many other treatments, is not specific to a particular type of tumour (e.g. hormone or HER2 positive tumours). This means it represents a treatment option for patients whose cancers do not respond to other targeted therapies. This may be of particular benefit in patients with forms of breast cancer that have more limited treatment options, such as those with triple negative breast cancer and patients who are HER2 negative as they have no other biological therapy available to them. However, the definition of a specified population will depend on the evidence obtained from clinical trials and there are clinical trials which have been conducted with bevacizumab and a non-taxane in both HER2 positive and HER2 negative patients.	Comment noted. The proposed marketing authorisation for bevacizumab in combination with non-taxane chemotherapy for the first-line treatment of metastatic breast cancer will be limited to people with HER2-negative disease only.
	Breast Cancer Care	The population in the draft appraisal is identified as those with metastatic breast cancer but will patients with stage3 (N3) disease be considered?	Comment noted. At this stage, bevacizumab in combination with non-taxane chemotherapy for the first-line treatment of metastatic breast cancer does not currently have a marketing authorisation. Guidance will only be issued in accordance with the marketing authorisation.
Comparators	**Breakthrough Breast Cancer**	Vinorelbine should also be considered a comparator when anthracyclines are unsuitable as monotherapy of either capecitabine or vinorelbine is recommended in this patient population (CG81).	Comment noted. Vinorelbine has been added as a comparator in the scope.

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	Breast Cancer Care	The listed comparators appear to be the ones available as current NHS treatment options and may also include trastuzumab in combination with paclitaxel.	Comment noted. The remit is to appraise bevacizumab in combination with non-taxane chemotherapy, therefore combination therapy with paclitaxel is outside the remit of this appraisal. Trastuzumab has a marketing authorisation for the treatment of patients with HER2 positive metastatic breast cancer. The proposed marketing authorisation for bevacizumab in combination with non-taxane chemotherapy for the first-line treatment of metastatic breast cancer will be limited to people with HER2-negative disease only.
Outcomes	**Breakthrough Breast Cancer**	It is important that the emphasis is placed on patient quality of life since advanced/metastatic breast cancer is a life limiting condition.	Comment noted. Health-related quality of life is an outcome measure included in the scope.
	Breast Cancer Care	Yes	Comment noted. No action required.
Economic analysis	**Breast Cancer Care**	When sufficient data is available from phase 3 trials.	Comment noted. No action required.

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Equality and Diversity	**Breast Cancer Care**	The equality issues relate to the use of bevacizumab as a first line treatment which, if not accepted by NICE, may be offered to patients in the private setting but not for NHS patients. The introduction of co-payments or 'top ups' is generally not widely taken up by patients and is often an option that patients find out about only when they have relapsed after first line treatments. If NICE does not approve this drug, people from lower socioeconomic groups will therefore be at a disadvantage and health inequalities will only widen as a result of the differences of access to this therapy.	Comment noted. NICE provides guidance to the NHS and its recommendations are based on clinical and cost-effectiveness. When formulating its recommendations, the Appraisal Committee considers the factors that are most appropriate to each appraisal. The Appraisal Committee takes into account legislation on human rights, discrimination and equality, and the directions from the Secretary of State. See Guide to the single technology appraisal process: http://www.nice.org.uk/media/913/06/Guide_to_the_STA-proof_6-26-10-09.pdf
Questions for consultation	**Breakthrough Breast Cancer**	A single technology appraisal would be the most suitable process for this technology. Responses to the other questions for consultations are covered in the draft scope comments.	Comment noted. NICE will appraise bevacizumab in combination with non-taxane chemotherapy for the first-line treatment of metastatic breast cancer using the single technology appraisal process.
	Breast Cancer Care	Response to consultation questions; -The population is defined in the scope as metastatic breast cancer patients. Breast Cancer Care would like to point out that as stage 3 patients may also need to be considered.	Comment noted. At this stage, bevacizumab in combination with non-taxane chemotherapy for the first-line treatment of metastatic breast

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			cancer does not currently have a marketing authorisation. Guidance will be issued in accordance with the marketing authorisation.
		The HER2 status should be stated based on the available study data which include HER2+ and HER2-patients.	Comment noted. The proposed marketing authorisation for bevacizumab in combination with non-taxane chemotherapy for the first-line treatment of metastatic breast cancer will be limited to people with HER2-negative disease only.
		-Vinorelbine would be a comparator when anthracycline is unsuitable but many patients appear to be offered capecitabine prior to this treatment option.	Vinorelbine has been added as a comparator in the scope.
		-The basal cell breast cancer or triple negative tumours may be expected to gain more benefit based on their limited treatment options.	As per the 'other considerations' section of the scope, potential subgroups such as by histology and hormone receptor status will be considered if evidence allows.
		-As mentioned the social equality concern is ensuring clinically appropriate treatments are available for all groups of patients irrespective of their ability to pay.	When formulating its recommendations, the Appraisal Committee considers the factors that are

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			most appropriate to each appraisal. The Appraisal Committee takes into account legislation on human rights, discrimination and equality, and the directions from the Secretary of State. See Guide to the single technology appraisal process: http://www.nice.org.uk/media/913/06/Guide_to_the_STA-proof_6-26-10-09.pdf
		The potential health benefits of bevacizumab and non- taxanes appears to be in the potential of delaying the time to disease progression in the first line treatment setting. This allows women with metastatic breast cancer to continue with most aspects of their normal daily life before the eventual progression of their disease and the associated debilitating symptoms and emotional distress this progression will bring. Maintaining the best quality of life for as long as possible is the most desirable outcome for this patient group.	Comment noted. No action required.
		-Trial E2100 and Avado may be of relevance in terms of the side effect profile. Any relevant date from phase 2(XCALIBr) trial with bevacizumab and xeloda accepting there may be further research in this first line treatment setting.	Comment noted. NICE seeks relevant evidence from several sources. See Guide to the single technology appraisal process: http://www.nice.org.uk/media/913/06/Guide_to_the_STA-proof_6-26-10-09.pdf
		- The single technology process would be most suitable for appraising this	NICE will appraise bevacizumab in combination

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		technology.	with non-taxane chemotherapy for the first-line treatment of metastatic breast cancer using the single technology appraisal process.
Additional comments on the draft scope.	**Breakthrough Breast Cancer**	It is essential that clinically effective drugs are available to all patients that may benefit from the drug, through the NHS. When this is not the case, Primary Care Trusts must make decisions regarding the prescription of drugs on an individual basis (exceptional case funding) and some patients may not, therefore, have access to the most effective treatments. With the decision to allow patients to supplement their NHS care ('top-up') further variation amongst the population could arise as for many patients this option will not be feasible.	Comment noted. NICE provides guidance to the NHS and its recommendations are based on clinical and cost-effectiveness. When formulating its recommendations, the Appraisal Committee considers the factors that are most appropriate to each appraisal. The Appraisal Committee takes into account legislation on human rights, discrimination and equality, and the directions from the Secretary of State. See Guide to the single technology appraisal process: http://www.nice.org.uk/media/913/06/Guide_to_the_STA-proof_6-26-10-09.pdf
	Breast Cancer Care	None	Comment noted. No action required.

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

1. **Breast Cancer Campaign**
2. **Roche**
3. **NHS Quality Improvement Scotland**

4. **Sanofi-Aventis**
5. **UK Oncology Nursing Society (UKONS)**
6. **Welsh Assembly Government**
7. **Royal College of Pathologists**
8. **Marie Curie Cancer Care**
9. **Department of Health**
10. **Cancer Network Pharmacists Forum**