National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Pertuzumab for the adjuvant treatment of HER2-positive breast cancer

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

Please note: 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.

Comment 1: the draft remit

Section	Consultee/ Commentator	Comments [sic]	Action
Wording	Roche	No comment	Response noted.
	Association of Breast Surgery	Yes	Comments noted.
Timing Issues	Roche	No comment	Response noted.
	Association of Breast Surgery	ABS feels that it would be appropriate for NICE to have an outcome of this appraisal within the next 6 months ideally or 12 months at the latest.	Comments noted. NICE aims to provide guidance to the NHS within 6 months from the date when the marketing authorisation for a technology is granted.

Section	Consultee/ Commentator	Comments [sic]	Action
Additional comments on the draft remit	Roche	None	Response noted.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information		Addition of wording in bold (for clarity): Breast cancer is described as 'early' if it is restricted to the breast, or the breast and nearby lymph nodes, and has not spread to other parts of the body (**i.e. at** clinical stages 1 and 2).	Comment noted. The scope has been updated to incorporate the suggestion.
The technology/ intervention	Roche	Incomplete information in paragraph 2 under 'The technology', page 1. Please add: *In addition to the marketing authorisation for neoadjuvant treatment, pertuzumab is also licensed in the UK for use in combination with trastuzumab and docetaxel in adult patients with HER2-positive metastatic or locally recurrent unresectable breast cancer, who have not received previous anti-HER2 therapy or chemotherapy for their metastatic disease.*	Comment noted. The subject of this appraisal is adjuvant treatment of early and locally advanced breast cancer, therefore reference to other breast cancer

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			indications have not been included.
Population	Roche	[redacted]	Comment noted. For a clear description of the population being considered in this appraisal, the phrase 'who have undergone surgery', is crucial.
Comparators	Roche	No comments	Response noted.
Outcomes	Roche	The outcome measures to be considered include: • invasive disease-free survival (IDFS) • IDFS with second non-breast primary cancers included • overall survival • disease-free survival • recurrence-free interval • distant recurrence-free interval • adverse effects of treatment and cardiac safety • health-related quality of life.	Comment noted. Disease-free survival has already been included in the scope. Further categorisation may be considered in the company's submission. The scope has been updated to include recurrence-free interval in the outcomes.

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	Association of Breast Surgery	If Quality of Life indicators are available in the literature that would be helpful in the discussion with patients should the pertuzamab be adopted into routine adjuvant clinical practice.	Comment noted. Guide to the methods of technology appraisal (2013) recommends health-related quality of life measured directly by patients in the relevant clinical trial. If not available, health-related quality of life data can be sourced from the literature.
Economic analysis	Roche	No comment	Response noted.
Equality and Diversity	Roche	No comment	Response noted.
Innovation	Roche	Despite the availability of HER2-targeted adjuvant treatment in HER2-positive early breast cancer (eBC), 51% of HER2-positive metastatic breast cancer cases are due to eBC relapse (246/484 patients evaluated in the SystHERs study). Clinical evidence from the APHINITY study demonstrate the benefits of dual HER2 blockade with adjuvant pertuzumab and trastuzumab in improving 3-year invasive disease-free survival (IDFS); the trend with improvements continuing at 4 years. Most benefit was noted in patients with	Comment noted. The innovative nature of pertuzumab will be considered by the NICE appraisal committee during the course of the appraisal.

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		additional risk factors such as node-positive and/or hormone-negative disease, demonstrating the benefits of adjuvant pertuzumab, trastuzumab and chemotherapy in high-risk patients. No additional safety signals or concerns were seen.	
Other considerations	Roche	No comment	Response noted.
	Association of Breast Surgery	Yes, this technology could potentially be of significant advantage to women with HER2+ve early stage breast cancer. Adjuvant pertuzumab improves early breast cancer outcomesDas, M. The Lancet Oncology 2017 epub Adjuvant Pertuzumab and Trastuzumab in Early HER2-Positive Breast Cancer. von Minckwitz G et al. N Engl J Med. 2017 Jun 5; . Epub 2017	Comment noted.
Questions for consultation	Roche	Q: Have all relevant comparators for pertuzumab been included in the scope? A: All relevant comparators have been included in the scope; chemotherapy regimens in combination with trastuzumab are considered to be established clinical practice in the NHS for the adjuvant treatment of HER2 positive, early or locally advanced breast cancer	Comment noted. If evidence allows, subgroups at higher risk of recurrence, such as people with lymph node positive disease or people with hormone receptor negative disease, will be

Section	Consultee/ Commentator	Comments [sic]	Action
		Q: Are the outcomes listed appropriate A: See above Q: Are there any subgroups of people in whom pertuzumab is expected to be more clinically effective and cost effective or other groups that should be examined separately? A: Patients with higher risk of recurrence, such as lymph node positive or hormone receptor negative disease, appear to derive the most benefit from the combination of pertuzumab and trastuzumab and chemotherapy Q: Where do you consider pertuzumab will fit into the existing NICE pathway? A: Pertuzumab will be added to where trastuzumab and chemotherapy will be indicated as part of adjuvant treatment for HER2+ eBC Q: Do you consider pertuzumab to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)? A: Please see innovation section above	considered, The scope has been updated. Comment noted. According to Guide to the methods of technology appraisal 2013, section 5.1.10 productivity costs cannot be included in either the reference-case or non-reference-case analyses.

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		Q: Do you consider that the use of pertuzumab can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation? A: Early treatment of breast cancer has a curative intent and, where successful, is likely to allow patients to return to their normal lives. Increasing the number of women who achieve a clinical cure/long-term remission, as achieved with the addition of pertuzumab to trastuzumab, is likely to result in wider societal benefits that are not captured by the QALY and NHS & PSS cost perspective. For example, a recent study (Verrill et al, publication-in-process) found that diagnosis & treatment has a significant impact on patients' work productivity, whether the patient was diagnosed with early or metastatic disease. Productivity was significantly improved for women who had completed systemic therapy for early breast cancer, however the productivity and ability to work for women with metastatic breast cancer is expected to continue to deteriorate as the disease advances. Q: Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year? A:	

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		METAPHER study: Phase IIIb Study to Evaluate the Safety and Tolerability of Herceptin SC with Perjeta and Docetaxel in Patients with HER2-positive Advanced Breast Cancer [redacted] BERENICE study: A Multicenter, Multinational, Phase II Study to Evaluate Pertuzumab in Combination With Trastuzumab and Standard Neoadjuvant Anthracycline-Based Chemotherapy in Patients With HER2-Positive, Locally Advanced, Inflammatory, or Early-Stage Breast Cancer [redacted]	
Additional comments on the draft scope	Roche	No comment	Response noted.

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

None