

Pertuzumab for the neoadjuvant treatment of HER2-positive breast cancer

Technology appraisal guidance
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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

1 Recommendations	4
2 The technology	5
Description of the technology	5
Marketing authorisation	5
Adverse reactions	5
Recommended dose and schedule	5
Price	6
3 Evidence	7
4 Committee discussion	8
Patient experience for people with HER2-positive breast cancer	8
Current clinical management of HER2-positive breast cancer	9
Clinical effectiveness	10
Cost effectiveness	14
Pharmaceutical Price Regulation Scheme (PPRS) 2014	18
5 Implementation	20
6 Appraisal committee members and NICE project team	21
Appraisal committee members	21
NICE project team	21

1 Recommendations

- 1.1 Pertuzumab, in combination with trastuzumab and chemotherapy, is recommended, within its marketing authorisation, as an option for the neoadjuvant treatment of adults with human epidermal growth factor receptor 2 (HER2)-positive breast cancer; that is, in patients with HER2-positive, locally advanced, inflammatory or early-stage breast cancer at high risk of recurrence. It is recommended only if the company provides pertuzumab with the discount agreed in the patient access scheme.

2 The technology

Description of the technology

- 2.1 Pertuzumab (Perjeta, Roche) is a recombinant monoclonal antibody which targets human epidermal growth factor receptor 2 (HER2)-positive breast tumours. It interrupts the activation of the HER2 intracellular signalling pathway, leading to cell growth arrest and apoptosis. It is administered by intravenous infusion.

Marketing authorisation

- 2.2 Pertuzumab has a marketing authorisation in the UK 'in combination with trastuzumab and chemotherapy for the neoadjuvant treatment of adult patients with HER2-positive, locally advanced, inflammatory, or early-stage breast cancer at high risk of recurrence'.

Adverse reactions

- 2.3 The summary of product characteristics includes the following adverse reactions for pertuzumab: decreased appetite, headache, cough, diarrhoea, vomiting, nausea, constipation, rash, pain, oedema, fatigue, asthenia and left ventricular dysfunction. For full details of adverse reactions and contraindications, see the summary of product characteristics.

Recommended dose and schedule

- 2.4 The recommended dosage of pertuzumab is an initial loading dose of 840 mg, followed by a maintenance dose of 420 mg every 3 weeks for 3 to 6 cycles.

Price

2.5 Pertuzumab costs £2,395 per 420-mg vial (excluding VAT).

The company has agreed a patient access scheme with the Department of Health. This scheme provides a simple discount to the list price of pertuzumab, 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

The [appraisal committee](#) considered evidence submitted by Roche and a review of this 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 pertuzumab, having considered evidence on the nature of HER2-positive breast cancer and the value placed on the benefits of pertuzumab by people with the condition, those who represent them, and clinical experts. It also took into account the effective use of NHS resources.

Patient experience for people with HER2-positive breast cancer

- 4.1 The committee heard from the patient expert that after having pertuzumab, she had experienced a complete response that her clinician described as 'spectacular'. She felt that taking pertuzumab not only had the benefit of removing the physical signs of cancer, but also had a major effect on her psychological wellbeing. When a person's tumour responds to treatment it can improve quality of life, and reassure them that the treatment is working. The clinical experts agreed that outcomes such as pathological complete response can have a strong psychological benefit for patients. They explained that pathological complete response is an indication that not only are tumour cells in the breast responding to treatment (and, in the case of total pathological response, that tumour cells in the lymph nodes are also responding to treatment), but that any tumour cells which may have already spread beyond the breast and nodes but that are undetectable (micro-metastases) would also have been treated. In addition, a reduction in size or the disappearance of tumour in the breast potentially allows for less radical surgery in patients who would otherwise be advised to have mastectomy. The committee agreed that neoadjuvant treatment outcomes such as pathological complete response seemed beneficial from a clinical perspective, and could provide important psychological benefits for patients. However, given the limitations of the evidence, it considered that there was uncertainty about whether a pathological complete response after neoadjuvant therapy was the sole and most reliable indicator of, or translated directly into, treatment-related long-term event-free and overall survival benefit ([section 4.5](#)). The committee also noted comments from Breast Cancer Now which indicated that although it considered pertuzumab to be a potentially

promising treatment, the charity strongly supported the collection of more evidence because many of the cited benefits are hypothetical. The committee concluded that HER2-positive breast cancer can have a substantial negative effect on quality of life, and that patients and clinicians place a strong value on effective early treatments that would be of particular value if they were proven to improve long-term outcomes.

Current clinical management of HER2-positive breast cancer

4.2 The committee heard from the clinical experts that there is variation across the NHS in the use of neoadjuvant therapy (primary systemic therapy) before surgery in HER2-positive breast cancer, which was demonstrated in an informal survey presented by one of the clinical experts. They stated that this may relate to service configuration issues, such as staffing levels and access to HER2 testing, and that this restricted access to neoadjuvant treatment in some parts of the UK. The clinical experts indicated that despite this variation, there is a trend in the NHS towards increasing use of neoadjuvant treatment for HER2-positive breast cancer, following the demonstrated survival benefits of HER2 agents given later in the disease pathway. In very extensive or inoperable disease, neoadjuvant treatment may shrink the tumour and make it operable. In other cases it may allow for breast-conserving surgery, thereby reducing the need for more complicated procedures (such as mastectomy and breast reconstruction) and their associated risks, lessening the treatment burden for both patients and the NHS. The clinical experts stated that another advantage of neoadjuvant treatment is that outcomes can be more directly linked to treatment (because there is less chance of confounding from other treatments), and that this was useful to inform future treatment decisions. The committee heard from the company and the ERG that around 75% of neoadjuvant treatment regimens for patients with HER2-positive cancers contain trastuzumab. The clinical experts stated there is variation in the chemotherapy given in combination with trastuzumab. The committee was interested in any disadvantages of neoadjuvant therapy, for example the potential for tumour growth before surgery. It heard from the clinical experts that it is extremely unlikely that a tumour would grow in size during neoadjuvant treatment, that patients are typically closely monitored,

including with MRI scans, so that any disease progression would be quickly identified. In most patients tumour shrinkage (albeit not necessarily total pathological response) is seen, and this can occur quite rapidly during a course of neoadjuvant treatment. The committee concluded that in current NHS practice there is a trend towards offering more neoadjuvant therapy in HER2-positive breast cancer, and that most neoadjuvant regimens in this patient group include trastuzumab.

Clinical effectiveness

Strength of clinical trial evidence

- 4.3 The company submitted evidence from 2 phase II randomised controlled trials relevant to the population in the scope, NeoSphere and TRYPHAENA. However, the committee considered both of these to have substantial limitations for the purposes of providing comparative effectiveness data for pertuzumab. Both trials were at an early stage of research (phase II) and lacked longer-term efficacy data, had small patient numbers, were open label, and were not powered for key outcomes of interest including progression-free survival and overall survival. The trial data were further limited because only 2 of the 4 arms in NeoSphere included licensed treatment combinations (arm A n=107, trastuzumab and docetaxel, and arm B, n=107, pertuzumab, trastuzumab and docetaxel), and because TRYPHAENA was a cardiac safety trial (so not primarily designed to test efficacy) and had pertuzumab in all 3 treatment arms with no control group. However, the committee agreed that despite these limitations, both trials contained data that helped to demonstrate the clinical effectiveness of pertuzumab. In NeoSphere there was a statistically significant increase in pathological complete response when pertuzumab was added to trastuzumab and docetaxel (both given every 3 weeks for 4 cycles; see section 4.4). TRYPHAENA included pathological complete response as a secondary outcome, and therefore provided additional supportive evidence. The committee concluded that the clinical trial evidence for pertuzumab in the neoadjuvant setting was limited, but in the absence of stronger evidence, results from NeoSphere could be used as the basis of its decision-making, supported by data from TRYPHAENA.

Results of clinical trial evidence

4.4 The committee noted that of the 3 available definitions of pathological complete response, the primary outcome in NeoSphere, pathological complete response in the breast, was the least stringent measure; it classified patients as responders even if there was residual disease in lymph nodes or ductal carcinoma in situ. Total pathological complete response, a secondary outcome in NeoSphere, is the preferred definition for regulatory purposes, which requires the disappearance of invasive cancer in the breast and lymph nodes (although in situ cancer in the breast may still be present). However, the committee noted that the addition of pertuzumab to trastuzumab plus docetaxel was associated with larger increases in all 3 definitions of pathological complete response than trastuzumab plus docetaxel alone (there was an absolute difference in pathological complete response of 16.8 to 20.6 percentage points between the 2 groups, depending on the definition). In addition, although there was no control arm, the TRYPHAENA trial also showed high rates of pathological complete response in all 3 pertuzumab treatment arms (total pathological complete response rates ranged from 57.3% to 66.2%). The committee also heard from 1 clinical expert who stated that the ability of pertuzumab to remove all cancer including ductal carcinoma in situ was 'remarkable', and it was also aware that the patient expert had a pathological complete response with pertuzumab that her clinician described as 'spectacular' ([section 4.1](#)). The committee accepted that the available evidence suggested that pertuzumab was an effective treatment to induce pathological complete response. However, it expressed concerns about the reliability of pathological complete response as a surrogate for longer-term survival outcomes for patients ([section 4.5](#)), and it noted that the trial was not powered for long-term outcomes. The committee concluded that there was evidence that pertuzumab could improve rates of pathological complete response when added to trastuzumab and docetaxel, but that there was no reliable trial evidence of event-free or overall survival benefit.

Association of pathological complete response with survival

4.5 The committee discussed the value of pathological complete response as a clinically meaningful indicator of longer-term event-free and overall survival. It was aware that a number of studies have been done to investigate this, including

the CTNeoBC meta-analysis, which the company had described in its submission and used in its modelling. CTNeoBC evaluated the prognostic value of pathological complete response, and found that at patient-level there was a correlation between pathological complete response and survival outcomes. However, at trial-level, CTNeoBC concluded that the evidence that a treatment-related improvement in pathological complete response translated into a treatment-related improvement in survival outcomes was very weak (correlation coefficients of 0.03 and 0.24 for event-free survival and overall survival respectively). The committee understood that correlation between 2 variables at an individual level does not necessarily imply that one can be used as a surrogate for the other when estimating the effect of a specific treatment. The committee was also aware that the ERG had reviewed the wider evidence in this area, and had stated that the evidence of a positive treatment effect translating into a positive effect on survival was not convincing. The committee agreed that there was considerable uncertainty about whether pathological complete response could be viewed as a surrogate marker of long-term benefit. However, it heard from the clinical experts that if a patient had a pathological complete response, they considered this to be a good indicator of long-term benefit, particularly in oestrogen receptor-negative tumours. The committee accepted that neoadjuvant pertuzumab was an effective treatment for inducing pathological complete response. It agreed that the evidence was limited with regard to long-term outcomes, but considered whether the outcome of pathological complete response may itself only be a marker of drug activity at a cellular or micro-metastatic level, and noted the improved overall survival demonstrated with the addition of pertuzumab in the CLEOPATRA trial in metastatic HER2-positive breast cancer. It was also aware that both the US Food and Drug Administration and the European Medicines Agency had concluded that it was 'reasonably likely' that pathological complete response was associated with improved survival outcomes. The committee was minded to accept that the complete disappearance of cancer in the breast and nodes was more likely to be associated with improved long-term outcomes than completely unrelated. On balance, although there was uncertainty about the exact relationship, the committee accepted that pathological complete response was more likely than not to have an association with longer-term survival. It concluded that despite the uncertainty, and in line with current oncological thinking, earlier HER2-specific treatment would have patient benefit in the long term, as well as the short-term benefit of tumour shrinkage or disappearance.

Generalisability of NeoSphere trial evidence to clinical practice in England

- 4.6 The committee noted that most patients in NeoSphere were described as having 'operable' disease (defined as tumours over 2 cm in diameter [T2 to 3] with no clinically involved lymph nodes [N0] or involved mobile ipsilateral axillary nodes [N1]), and that people in this category would have the best prognosis of the 3 subgroups in the trial (that is, operable, locally advanced and inflammatory). In addition, the low patient numbers in the trial resulted in one of the rare subtypes, inflammatory breast cancer, having only 7 patients in the comparator arm and 10 patients in the intervention arm. The committee considered that there were likely to have been very few UK patients in the trial; only 214 patients had either the intervention or comparator as stated in the scope, across 59 centres, and of these only 2 centres were in the UK. However, the committee agreed that the comparator used reflected current NHS practice, because 75% of neoadjuvant treatment regimens in the UK include trastuzumab. Furthermore, in response to the appraisal consultation document, the company had stated that clinical expert opinion supported the generalisability of the clinical trial evidence, although it did not provide any supporting evidence. The committee concluded that although there was some uncertainty about the generalisability of the NeoSphere trial to current NHS practice, it was appropriate for decision-making.

Adverse events associate with pertuzumab

- 4.7 The committee noted that TRYPHAENA was specifically designed to assess the cardiac safety of pertuzumab. However, the committee considered 1 of the 2 primary outcomes used to measure cardiac safety, left ventricular systolic dysfunction, to be a poor indicator of cardiac safety. The committee noted that adverse events in NeoSphere were similar in both the intervention and comparator arms. The committee also heard from the patient expert who found the effects of pertuzumab to be very manageable, with the only notable effects being diarrhoea and a slower than expected return to normal hair growth. The committee concluded that based on the evidence, pertuzumab had an acceptable adverse event profile.

Cost effectiveness

Health economic model: structure and parameter assumptions

4.8 Although the locoregional recurrence health state omitted surgery (which would be the best option for patients at this stage of the treatment pathway), the committee considered the general structure of the model and sequencing of health states to be plausible. However, it had concerns about the parameter assumptions used in the model for effectiveness ([section 4.9](#)) and costs ([section 4.11](#)). Furthermore, the committee expressed concern that in September 2015 the company had submitted to the Scottish Medicines Consortium (SMC) for consideration of pertuzumab for the same indication. In the SMC submission, the company had derived substantially different incremental costs, utility values and cost-effectiveness results to those submitted to NICE, but had not provided a full and clear explanation of the reasons for the differences. In response to the appraisal consultation document, the company provided a detailed explanation which more clearly demonstrated that the main difference between the 2 submissions was the incorporation of costs of drugs funded by the Cancer Drugs Fund (CDF), which were available in England but not Scotland. Although the committee regretted that this uncertainty had not been resolved earlier, it welcomed this additional transparency from the company, which helped to reassure the committee at its second meeting that none of the variation was a cause for concern. The committee was satisfied it now understood the reasons for the variation between the NICE and SMC incremental cost-effectiveness ratios (ICERs), and concluded that the structure of the model was generally appropriate for decision-making, although it was still subject to uncertainty because of some parameter assumptions.

Health economic model: clinical-effectiveness assumptions

4.9 The company assumed that pathological complete response was a surrogate for survival in the model, because the event-free survival data from the trial were not robust enough to be used in the model. The committee was aware that the [NICE guide to the methods of technology appraisal](#) contains guidance on the use of surrogate outcomes within health economic models, stating that: 'evidence in

support of the surrogate-to-final end point outcome relationship must be provided together with an explanation of how the relationship is quantified for use in modelling'. The committee noted that the company had attempted to provide evidence to support the relationship using the CTNeoBC meta-analysis. This study identified a patient-level relationship between pathological complete response and survival, but could not validate pathological complete response as a valid surrogate for survival. The committee was aware of the authors' conclusions that there were several possible reasons for the lack of proof of surrogacy, including low overall pathological complete response rates, heterogeneous patient populations, and inclusion of only a single study designed to evaluate effects of targeted therapy. The committee also considered that it may be difficult to prove this relationship because pathological complete response was a binary outcome (response or no response), whereas in clinical practice, the outcome may be more nuanced; it is possible that the proportion of individual patient response may affect long-term outcomes without necessarily meeting the threshold to be classified as a response in the trial. The committee noted that the company had attempted to explore uncertainty in this area with a scenario analysis using the less robust survival data from NeoSphere, which improved the cost-effectiveness results for pertuzumab. Overall, in the absence of an alternative source of robust effectiveness data and taking into account that it considered that pathological complete response was more likely than not to be associated with longer-term outcomes ([section 4.5](#)), the committee concluded that the company's approach to model clinical effectiveness was acceptable. However, it was subject to high levels of uncertainty, and the committee would need to interpret any survival estimates with caution.

Health economic model: health-related quality-of-life assumptions

- 4.10 The committee discussed differences in the quality-adjusted life year (QALY) gains in the SMC and NICE company submissions (0.31 in the SMC submission, 0.261 in the NICE submission). It also discussed the differences in the utility value for the progressed state used in the model (0.5 in the SMC submission, 0.452 in the NICE submission). The committee heard from the company that some of the difference in QALY gains was because it had added an extra assumption to the model submitted to NICE, specifically that the utility value could not be higher

than the age-matched population without disease. The company also explained that it used a lower utility value in the NICE submission because it considered a study by Lloyd et al. (2006) to provide a more appropriate utility measure. The company did not explain why it considered a different utility value from that used in the SMC submission to be appropriate. At the first appraisal committee meeting, the committee could not be sure of the effect of these differences because the company had not provided sufficient explanation. However, in response to the appraisal consultation document, the company supplied a more detailed explanation of the main differences and their effects. The committee accepted this explanation and concluded that the health-related quality of life assumptions used in the NICE model were appropriate for decision-making.

Health economic model: cost assumptions

- 4.11 The committee discussed whether the inclusion of drugs funded by the CDF in the metastatic health states was a fair reflection of the future costs of treatment for HER2-positive breast cancer in England. The committee noted that by including these drugs, the additional costs of neoadjuvant pertuzumab were being offset in the model by the costs of additional drugs for metastatic disease in the comparator arm funded by the CDF (including pertuzumab and trastuzumab emtansine). The committee was aware that the CDF is a temporary funding vehicle for cancer drugs that cannot yet demonstrate cost effectiveness, and is currently in a transitional period to determine which drugs should be funded. For patients starting neoadjuvant treatment today, the costs of treatment for metastatic disease (if needed) are likely to be incurred several years in the future, by which time there is no guarantee that the CDF will still be operating in the same way. The committee was aware that in modelling the future costs and benefits of treatments, there is always an element of uncertainty. However, given the transitional nature of the CDF, the committee questioned the validity of the large cost offsets assumed by the company. The committee also noted the ERG's comment that the company had incorporated pertuzumab as a second-line metastatic treatment in the model, although its licence is for use in combination with trastuzumab and docetaxel in patients who have not had previous anti-HER2 therapy or chemotherapy for their metastatic disease. Furthermore, the committee raised concerns about the company's precise drug costs. The company used list prices for the CDF-funded treatments, but the NHS may be

paying lower prices for these drugs which would increase the ICER. In its response to the appraisal consultation document, the company provided various scenario analyses that changed assumptions for the drugs funded by the CDF, including using actual costs currently paid by the NHS for these drugs, and completely removing CDF-funded treatments. Furthermore, in order to mitigate the risks of any future changes to the CDF, the company submitted a confidential simple discount patient access scheme. The committee appreciated the company's attempt to resolve the uncertainty both with the presentation of additional scenario analyses, and the offer to risk-share against any changes in CDF-funded treatments by reducing the costs of pertuzumab. It concluded that this helped to reduce uncertainty in the cost-effectiveness results.

Incremental cost-effectiveness results

4.12 The committee considered the cost-effectiveness results presented by the company and the ERG. It noted that in the original company submission and ERG report, there were a number of different base-case scenarios, but that all were subject to uncertainty. Particular issues of relevance included assumptions about the future costs and availability of CDF-funded treatments, and also effectiveness assumptions. In exploratory analyses, both the company and ERG models were most sensitive to assumptions about clinical effectiveness (that is, assumptions about the rates of pathological complete response, which influenced survival estimates in the model). However, the committee accepted that there was evidence that rates of pathological complete response were statistically significantly higher with the addition of pertuzumab to trastuzumab and docetaxel ([section 4.4](#)), and that correspondingly high rates of pathological complete response had also been demonstrated in the TRYPHAENA trial. With respect to costs and availability of CDF drugs in the metastatic setting, the company had attempted to address uncertainty in scenario analyses ([section 4.11](#)). The committee agreed that because of the high levels of uncertainty in the cost-effectiveness assumptions, it would be prudent to use the more conservative ICERs from the ERG, and to focus on scenarios which excluded any cost offsets from metastatic treatments funded by the CDF. The committee noted that in these more conservative scenarios, and incorporating the simple discount patient access scheme for pertuzumab, the ICERs fell within the range normally considered to be a cost-effective use of NHS resources. The

committee noted that the comparatively early regulatory approval for pertuzumab had limited the clinical trial evidence available such that it was suboptimal for the purposes of long-term modelling and health technology assessment. In these uncertain circumstances, the committee welcomed the company's approach to discount the cost of pertuzumab as it increased the likelihood that pertuzumab would be cost effective with more conservative assumptions than had been used in the model. The committee concluded that pertuzumab could be recommended as a cost-effective use of NHS resources for the neoadjuvant treatment of HER2-positive breast cancer.

- 4.13 The committee discussed whether it would be appropriate to specify the number of cycles of pertuzumab that should be used in clinical practice. It was aware that the NeoSphere trial and the model used 4 cycles, but that the licence allowed for 3 to 6 cycles, which was a large variation (effectively meaning that for some patients dosage and costs could be double that of others). It heard from the clinical experts that they would use pertuzumab for 3 to 6 cycles but that this would vary. One clinical expert stated that the clinical effect of 3 cycles was probably the same as the effect after 6 cycles. The committee noted that the ERG had done a sensitivity analysis (without the patient access scheme discount) varying the number of cycles of pertuzumab, which caused the ICER to increase from £23,467 per QALY gained (ERG's base case, based on 4 cycles of pertuzumab) to £42,955 per QALY gained (using 6 cycles of pertuzumab and amending the costs but not the effectiveness of treatment), suggesting that the results were sensitive to this assumption. The committee concluded that patients should normally have no more than 4 cycles of neoadjuvant treatment with pertuzumab.

Pharmaceutical Price Regulation Scheme (PPRS) 2014

- 4.14 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.

5 Implementation

- 5.1 Section 7(6) 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 HER2-positive breast cancer and the doctor responsible for their care thinks that pertuzumab is the right treatment, it should be available for use, in line with NICE's recommendations.
- 5.4 The Department of Health and Roche have agreed that pertuzumab will be available to the NHS with a patient access scheme which makes it available with a discount. The size of the discount is commercial in confidence. It is the responsibility of the company to communicate details of the discount to the relevant NHS organisations. Any enquiries from NHS organisations about the patient access scheme should be directed to global.pas@roche.com.

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.

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