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## **Trastuzumab for the adjuvant treatment of early- stage HER2-positive breast cancer**

**This guidance was developed using the  
Single Technology Appraisals process.**

## **NICE technology appraisal guidance 107 Trastuzumab for the adjuvant treatment of early-stage HER2-positive breast cancer**

### **1.1.1 Ordering information**

You can download the following documents from [www.nice.org.uk/TA107](http://www.nice.org.uk/TA107)

- The full guidance (this document).
- A quick reference guide for healthcare professionals.
- Information for women with breast cancer and their carers ('Understanding NICE guidance').
- Details of all the evidence that was looked at and other background information.

For printed copies of the quick reference guide or 'Understanding NICE guidance', phone the NHS Response Line on 0870 1555 455 and quote:

- N1111 (quick reference guide)
- N1112 ('Understanding NICE guidance').

### **1.1.1 This guidance is written in the following context**

This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

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## 1 Guidance

- 1.1 Trastuzumab, given at 3-week intervals for 1 year or until disease recurrence (whichever is the shorter period), is recommended as a treatment option for women with early-stage HER2-positive breast cancer following surgery, chemotherapy (neoadjuvant or adjuvant) and radiotherapy (if applicable).
- 1.2 Cardiac function should be assessed prior to the commencement of therapy and trastuzumab treatment should not be offered to women who have a left ventricular ejection fraction (LVEF) of 55% or less, or who have any of the following:
- a history of documented congestive heart failure
  - high-risk uncontrolled arrhythmias
  - angina pectoris requiring medication
  - clinically significant valvular disease
  - evidence of transmural infarction on electrocardiograph (ECG)
  - poorly controlled hypertension.
- 1.3 Cardiac functional assessments should be repeated every 3 months during trastuzumab treatment. If the LVEF drops by 10 percentage (ejection) points or more from baseline and to below 50% then trastuzumab treatment should be suspended. A decision to resume trastuzumab therapy should be based on a further cardiac assessment and a fully informed discussion of the risks and benefits between the individual patient and their clinician.

## 2 The technology

- 2.1 Trastuzumab (Herceptin, Roche Products) is a recombinant humanised IgG1 monoclonal antibody directed against the human epidermal growth factor receptor 2 (HER2). Trastuzumab is licensed for the treatment of patients with early-stage HER2-positive breast cancer, following surgery, chemotherapy (adjuvant or neoadjuvant) and radiotherapy (if applicable). Trastuzumab

should only be used in patients whose tumours have either HER2 overexpression or HER2 gene amplification as determined by an accurate and validated assay.

- 2.2 Trastuzumab is associated with cardiotoxicity. The 'Summary of product characteristics' (SPC) states that treatment cannot be recommended for patients with a history of documented congestive heart failure, high-risk uncontrolled arrhythmias, angina pectoris requiring medication, clinically significant valvular disease, evidence of transmural infarction on ECG or poorly controlled hypertension, because these patient groups were excluded from the registration study. The SPC also states that caution should be taken in treating patients with symptomatic heart failure, a history of hypertension, documented coronary artery disease or an LVEF of 55% or less. For full details of the side effects and contraindications, see the SPC.
- 2.3 Trastuzumab is licensed as an intravenous infusion given at intervals of either 1 or 3 weeks (once-weekly or 3-weekly dosing regimens). The 3-weekly regimen is given as an initial loading dose of trastuzumab at 8 mg/kg body weight followed by 6 mg/kg every 3 weeks for 1 year. The once-weekly regimen is given as a 4 mg/kg loading dose followed by 2 mg/kg every week for 1 year. The once-weekly regimen is licensed to be given concurrently with paclitaxel. The net price of a 150 mg vial of trastuzumab is £407.40 (excluding VAT; British national formulary 50). Assuming that 70% of patients will weigh 75 kg or less and there is vial wastage, the average cost per person of the 3-weekly regimen is £24,600 (excluding VAT) and the average cost of the once-weekly regimen is £28,000 (excluding VAT). Costs may vary in different settings because of negotiated procurement discounts.

### **3 The manufacturer's submission**

The Appraisal Committee (appendix A) considered evidence submitted by the manufacturer of trastuzumab and a review of this submission by the evidence review group (appendix B).

- 3.1 The manufacturer's submission compared trastuzumab following surgery and standard adjuvant treatment with surgery followed by standard adjuvant treatment alone. Standard adjuvant treatment was defined as chemotherapy without trastuzumab (plus locoregional radiotherapy and systemic hormonal treatment, where appropriate). In the decision problem trastuzumab was given over 1 year using the 3-weekly dosing schedule used in the HERA registration trial. The economic modelling was also based on this 3-weekly dosing schedule. The manufacturer responded to a request for clarification from NICE once the SPC was available and provided additional estimates of cost effectiveness for the once-weekly dosing schedule used in other trastuzumab trials. The primary outcome was disease-free survival and secondary outcomes were overall survival, relapse-free survival and distant disease-free survival.
- 3.2 The manufacturer's submission included a systematic review which identified five randomised controlled trials of trastuzumab in the adjuvant setting. One study (HERA) was considered to provide the primary source of evidence. In this study women had surgery and completed standard chemotherapy before they were entered into the study and randomly allocated to receive either no treatment or trastuzumab once every 3 weeks for either 1 or 2 years (N=5090). The results of the HERA study showed 87.1% of patients in the control arm and 92.5% of patients in the trastuzumab arm free from disease at 1 year follow up, equating to a 46% relative reduction in the risk of recurrence (hazard ratio (HR): 0.54, 95% CI: 0.44 to 0.67). In terms of overall survival 97.6% of patients in the control arm and 98.2% of patients in the trastuzumab arm were alive at 1 year follow up, equating to a 24% relative reduction in mortality (HR: 0.76, 95% CI: 0.47 to 1.23) for patients taking trastuzumab. The incidence of serious cardiac adverse events was 0.6% in the trastuzumab arm versus 0.1% in the control arm (HR not reported).
- 3.3 Three additional studies (NCCTG N9831, NSABP B-31, BCIRG 006) were identified in the submission as providing supporting evidence because the chemotherapy regimen used (including a taxane) was not considered by the

manufacturer to reflect current standard care in England and Wales. Another trial (FinHer) was excluded from the systematic review because of small patient numbers (N=231), because the chemotherapy regimens used were not considered to reflect current standard care and because trastuzumab was given at a dosing schedule different from the licensed regimen (FinHer used a weekly regimen for 3 months).

- 3.4 The estimates of cost effectiveness provided by the manufacturer were based on data from the HERA trial using the 3-weekly regimen of trastuzumab. The economic model was a state transition model that compared the lifetime impact of adding 1 year of trastuzumab therapy to standard care with standard care alone. The manufacturer's initial cost effectiveness estimate was £5,687 per additional quality-adjusted life year (QALY) gained. One-way sensitivity analyses carried out by the manufacturer found that this estimate varied from £2,834 to £8,689 per additional QALY gained. The base-case estimate of cost effectiveness was subsequently revised by the manufacturer following a request for clarification from NICE on behalf of the evidence review group. A further revision to the model structure was also made independently by the manufacturer. The manufacturer's revisions resulted in an estimated incremental cost per additional QALY gained of £2,387. After further clarification a base-case cost effectiveness estimate of £3,433 per additional QALY gained was submitted for the once-weekly dosing schedule.
- 3.5 The evidence review group identified no further studies of trastuzumab as an adjuvant treatment for early-stage HER2-positive breast cancer. The evidence review group noted that disease-free survival was the primary outcome used in all the studies identified in the manufacturer's submission. Gains in overall survival had not been observed in a number of studies because the duration of follow-up was short. In addition a wide variety of chemotherapy regimens had been used in the studies, although the evidence review group noted consistency of relative effect across the clinical trials. The evidence review group conducted a meta-analysis of the data from all five trastuzumab studies, where it was available. This showed that the addition of trastuzumab

led to a 33% relative improvement in overall survival (HR: 0.67, 95% CI: 0.52 to 0.87) and a 50% relative improvement in disease-free survival (HR: 0.50, 95% CI: 0.44 to 0.77). Studies also showed a relative increase in grades 3 and 4 cardiac toxicity of 550% (relative risk (RR) 5.54, 95% CI: 2.07 to 14.82), although this reflects an absolute increase of 1.6%.

- 3.6 The evidence review group highlighted a number of assumptions behind the manufacturer's economic model that may be optimistic and could mean that the incremental costs per QALY gained were underestimated. The evidence review group reviewed the literature and consulted clinical specialists to identify alternative assumptions which the manufacturer was requested to incorporate into its sensitivity analyses. However, these additional analyses did not materially change the estimates of cost effectiveness. The evidence review group then developed a number of scenarios that reflected alternative assumptions. Using the manufacturer's model, they altered the proportion of women receiving trastuzumab in the metastatic setting to better reflect the advice on likely use in clinical practice and shortened the duration of benefit obtained from trastuzumab. This resulted in an estimate of approximately £18,000 per additional QALY gained for the 3-weekly regimen. Other scenarios modelled on this estimate gave incremental costs per QALY gained ranging from £16,000 to £33,000.
- 3.7 Full details of all the trials are in the manufacturer's submission and evidence review group report, which are available from [www.nice.org.uk/TA107](http://www.nice.org.uk/TA107)

## **4 Consideration of the evidence**

- 4.1 The Committee (appendix A) reviewed the data available on the clinical and cost effectiveness of trastuzumab, having considered evidence (appendix B) on the nature of the condition and the value placed on the benefits of trastuzumab by people with early-stage HER2-positive breast cancer, those who represent them, and clinical experts. It was also mindful of the need to take account of the effective use of NHS resources.

- 4.2 The Committee considered that the decision problem had been adequately specified in the manufacturer's submission. The Committee noted that the manufacturer's submission had focused on the total population of women with early-stage breast cancer and had included the costs of HER2 testing for this entire group in their economic analyses. It noted that after a request from NICE the manufacturer submitted cost-effectiveness analyses based on the once-weekly dosing schedule. The Committee noted that the use of trastuzumab after neoadjuvant chemotherapy was licensed but had not been specified in the manufacturer's decision problem. However, the Committee was aware that evidence from the registration trial would enable them to make recommendations on the use of trastuzumab following neoadjuvant chemotherapy and it was satisfied that this did not need to be considered separately.
- 4.3 The Committee reviewed the evidence regarding the clinical effectiveness of trastuzumab as an adjuvant treatment for early-stage HER2-positive breast cancer. The Committee accepted that trastuzumab had been shown to reduce the risk of recurrence of HER2-positive breast cancers. The Committee was concerned that the short-term follow-up of all the trials meant that there was only limited evidence about gains in overall survival, and whether trastuzumab reduced recurrences or delayed them. However, it heard from clinical specialists that the relationship between prevention of early recurrence and overall survival benefit seen in clinical trials with other breast cancer drugs could be extrapolated to the patient group eligible for trastuzumab. It also heard from clinical specialists that, on this basis, breast cancer recurrence was likely to be reduced rather than delayed. The Committee therefore accepted that measures of disease-free survival could be used as a surrogate for overall survival.
- 4.4 The Committee considered the different adjuvant chemotherapy regimens used in the trastuzumab studies in the context of current practice in England and Wales. The Committee noted that trastuzumab treatment led to similar relative risk reductions when added to a range of different chemotherapy

regimens. The Committee was persuaded that there was sufficient comparability with current practice in England and Wales for the results of the trastuzumab trials to be considered generalisable. However, the Committee was mindful of the impact on cost effectiveness of differences in baseline risk of recurrence for patients treated with different adjuvant chemotherapy regimens.

- 4.5 The Committee considered carefully the available evidence relating to the cardiotoxicity associated with trastuzumab treatment. The Committee was aware that the HERA registration study had excluded women with an LVEF of 55% or less, and that other studies that had included such women had shown a higher rate of cardiac adverse events, in particular congestive heart failure. The Committee noted that women with a range of cardiac conditions had been excluded from the HERA study and that extensive cardiac screening and monitoring was required before and during trastuzumab treatment. The Committee acknowledged that the short-term follow-up of the HERA trial meant that the longer-term risks of trastuzumab therapy even in this restricted population were not fully known, and expressed concern that in another adjuvant trastuzumab study (BCIRG 006) longer-lasting cardiotoxic side effects had been observed in some women. The Committee concluded that while the short-term cardiotoxicity associated with trastuzumab had been evaluated, uncertainties remained over long-term effects and the possible impact of trastuzumab therapy in women with a range of cardiac conditions or an LVEF of 55% or less.
- 4.6 The Committee noted that, as stated in the SPC, the efficacy of trastuzumab had not been demonstrated in women with both node-negative disease and a primary tumour size of less than or equal to 1 cm because this group of patients was excluded from all of the trastuzumab studies and considered to be at low risk of recurrence. The Committee appreciated that although the overall long-term prognosis for women with HER2-positive tumours was worse than for those with HER2-negative status, other factors also influenced long-term prognosis. Thus for some women with HER2-positive tumours (that

is, those with node-negative disease and small primary tumours) there was a lower risk of recurrence. Therefore the absolute benefit these women would gain from trastuzumab treatment would be smaller than for the group as a whole. In these circumstances the side effects associated with trastuzumab (specifically cardiotoxicity) may outweigh the benefits. Evidence from clinical specialists indicated that in current clinical practice in England and Wales only women considered to be at a higher risk of recurrence would be offered adjuvant chemotherapy. The Committee was therefore satisfied that the group of HER2-positive women normally considered eligible for adjuvant chemotherapy in England and Wales would be equivalent to those patients shown to achieve benefit from trastuzumab in the main registration study.

- 4.7 The Committee reviewed the evidence on the cost effectiveness of trastuzumab. It was aware that limitations in the evidence base meant that a number of assumptions were made in the manufacturer's economic model. The Committee heard that as yet there is no evidence from trastuzumab trials of the duration of benefit following 1 year of trastuzumab treatment. It reflected that, on the basis of evidence from trials of other chemotherapy agents for high-risk early-stage breast cancers, the assumption of a lifetime benefit made in the manufacturer's model was likely to be optimistic and that a more conservative assumption would be 5 years of clinical benefit. In addition the Committee heard from the clinical specialists that the assumption by the manufacturer that women who had received trastuzumab in the adjuvant setting would not then receive trastuzumab in the metastatic setting was unlikely to reflect clinical practice. The Committee concluded that, based on these assumptions, the incremental cost per QALY estimate of £2,387 in the manufacturer's submission was likely to be underestimated and that the evidence review group's estimate of £18,000 was more likely to reflect the cost effectiveness of trastuzumab. However, it was mindful that the latter was also associated with uncertainty and that the alternative assumption that 100% of patients would be re-treated with trastuzumab for metastatic breast

cancer, as proposed by the evidence review group, was also unlikely to fully reflect clinical practice.

- 4.8 The Committee considered the differences between the once-weekly and 3-weekly dosing schedules. They noted that the manufacturer's submission had been based on the 3-weekly dosing schedule, although an estimate for cost per QALY gained was later provided for the once-weekly dosing schedule. They noted that the once-weekly dosing schedule was not strictly comparable with the 3-weekly schedule because on the basis of the licence it incorporated the concurrent use of paclitaxel. The Committee then considered the higher administration and drug costs associated with the once-weekly regimen and heard from clinical specialists that they would prefer to offer a 3-weekly regimen. The Committee was therefore satisfied that the once-weekly regimen would not be an appropriate use of NHS resources relative to the 3-weekly regimen.
- 4.9 The Committee then considered how cardiac adverse events had been included in the cost-effectiveness estimates from the manufacturer. In the manufacturer's model it was assumed that severe (grade 3 and 4) and less severe (grade 1 and 2) cardiac adverse effects occurred at the same rate as in the HERA trial and only occurred during treatment with trastuzumab. In addition, the model assumed there was no mortality associated with any cardiac event in either the short or long term. Therefore the Committee considered that the manufacturer's model underestimated both the costs and the reduction in quality of life associated with the treatment of possible long-term effects of cardiotoxicity. The Committee considered the sensitivity analysis carried out by the evidence review group that assumed that 23% of women would experience a cardiac event following treatment with trastuzumab, as is known to occur with anthracycline-including chemotherapy regimens. All other assumptions were maintained in the analysis. The Committee noted that the resulting estimate of cost per QALY gained would be approximately £33,000 and that this also assumed no excess mortality.

4.10 The Committee was mindful that the favourable cost per QALY estimates could have been a function of the extensive cardiac screening, monitoring and treatment discontinuation rules used in the HERA study before and during trastuzumab treatment which would therefore need to be replicated in clinical practice. The Committee was also aware of the possibility that, although no direct evidence was presented, estimates of cost per QALY gained for those patients with significant cardiac risk factors who were excluded from the registration trial, in particular women with an LVEF of 55% or less, could reasonably be assumed to be higher than both the manufacturer's estimates and the base-case suggested by the evidence review group. The Committee concluded that on this basis it would not be able to recommend trastuzumab for patients who have an LVEF of 55% or less or one of a documented range of cardiac conditions as specified in the exclusion criteria of the registration trial and identified in the SPC.

## **5 Implementation**

5.1 The Healthcare Commission assesses the performance of NHS organisations in meeting core and developmental standards set by the Department of Health in 'Standards for better health' issued in July 2004. The Secretary of State has directed that the NHS provides funding and resources for medicines and treatments that have been recommended by NICE technology appraisals normally within 3 months from the date that NICE publishes the guidance. Core standard C5 states that healthcare organisations should ensure they conform to NICE technology appraisals.

5.2 'Healthcare Standards for Wales' was issued by the Welsh Assembly Government in May 2005 and provides a framework both for self-assessment by healthcare organisations and for external review and investigation by Healthcare Inspectorate Wales. Standard 12a requires healthcare organisations to ensure that patients and service users are provided with effective treatment and care that conforms to NICE technology appraisal guidance. The Assembly Minister for Health and Social Services issued a

Direction in October 2003 which requires Local Health Boards and NHS Trusts to make funding available to enable the implementation of NICE technology appraisal guidance, normally within 3 months.

5.3 NICE has developed tools to help organisations implement this guidance (listed below). These are available on our website ([www.nice.org.uk](http://www.nice.org.uk)).

- Costing report and costing template to estimate the savings and costs associated with implementation.
- Audit criteria to monitor local practice.

## **6 Recommendations for further research**

6.1 The Committee considered that further investigation in the following areas would be valuable.

- Randomised controlled trials (RCTs) that investigate the impact of shorter trastuzumab treatment periods on clinical effectiveness and adverse events.
- RCTs that investigate the optimal scheduling of trastuzumab treatment with different chemotherapy regimens.
- Long-term follow-up of women who have been treated with trastuzumab.
- Studies that examine the risk of recurrence in specific subgroups (for example, those with nodal involvement, those with tumours with and without hormone receptors).

## 7 Related guidance

7.1 NICE has issued the following related clinical guideline:

- Familial breast cancer: the classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care. *NICE clinical guideline* no. 14 (May 2004). Available from: [www.nice.org.uk/CG014](http://www.nice.org.uk/CG014)

7.2 In 2002, NICE issued guidance on the use of trastuzumab for the treatment of metastatic breast cancer in patients whose tumours overexpress HER2.

- Guidance on the use of trastuzumab for the treatment of advanced breast cancer. *NICE technology appraisal* no. 34 (March 2002). Available from [www.nice.org.uk/TA034](http://www.nice.org.uk/TA034)

7.3 NICE is in the process of producing the following technology appraisals:

- Docetaxel for the adjuvant treatment of early node-positive breast cancer (publication expected September 2006).
- Paclitaxel for the adjuvant treatment of early node-positive breast cancer (publication expected September 2006).
- Hormonal therapies for early breast cancer (publication expected November 2006).

7.4 NICE is in the process of producing the following clinical guidelines:

- Familial breast cancer: the classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care (partial update of CG14; publication expected October 2006).
- Breast cancer: diagnosis and treatment (publication expected July 2008).

## **8 Review of guidance**

- 8.1 The review date for a technology appraisal refers to the month and year in which the Guidance Executive will consider whether the technology should be reviewed. This decision will be taken in the light of information gathered by the Institute, and in consultation with consultees and commentators.

The guidance on this technology will be considered for review in June 2007.

Andrew Dillon  
Chief Executive  
August 2006

## **Appendix A. Appraisal Committee members and NICE project team**

### **A. Appraisal Committee members**

The Appraisal Committee is a standing advisory committee of the Institute. Its members are appointed for a 3-year term. A list of the Committee members who took part in the discussions for this appraisal appears below. The Appraisal Committee meets twice a month except in December, when there are no meetings. The Committee membership is split into two branches, with the chair, vice chair and a number of other members attending meetings of both branches. Each branch considers its own list of technologies and ongoing topics are not moved between the branches.

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.

#### **Dr Jane Adam**

Radiologist, St George's Hospital, London

#### **Professor A E Ades**

MRC Senior Scientist, MRC Health Services Research Collaboration, Department of Social Medicine, University of Bristol

#### **Dr Amanda Adler**

Consultant Physician, Cambridge University Hospitals Fund, Cambridge

#### **Dr Tom Aslan**

General Practitioner, Stockwell, London

**Professor David Barnett (Chair)**

Professor of Clinical Pharmacology, University of Leicester

**Mrs Elizabeth Brain**

Lay Member

**Dr Peter I Clark**

Consultant Medical Oncologist, Clatterbridge Centre for Oncology, Merseyside

**Dr Karl Claxton**

Health Economist, University of York

**Dr Richard Cookson**

Senior Lecturer in Health Economics, School of Medicine Health Policy and Practice, University of East Anglia

**Mrs Fiona Duncan**

Clinical Nurse Specialist, Anaesthetic Department, Blackpool Victoria Hospital, Blackpool

**Dr Paul Ewings**

Statistician, Taunton & Somerset NHS Trust, Taunton

**Professor John Geddes**

Professor of Epidemiological Psychiatry, University of Oxford

**Mr John Goulston**

Director of Finance, Barts and the London NHS Trust

**Mr Adrian Griffin**

Health Outcomes Manager, Johnson & Johnson Medical Ltd

**Ms Linda Hands**

Consultant Surgeon, John Radcliffe Hospital

**Dr Elizabeth Haxby**

Lead Clinician in Clinical Risk Management, Royal Brompton Hospital

**Dr Rowan Hillson**

Consultant Physician, Diabeticare, The Hillingdon Hospital

**Dr Catherine Jackson**

Clinical Senior Lecturer in Primary Care Medicine, University of Dundee

**Professor Richard Lilford**

Professor of Clinical Epidemiology, Department of Public Health and Epidemiology, University of Birmingham

**Dr Simon Mitchell**

Consultant Neonatal Paediatrician, St Mary's Hospital, Manchester

**Ms Judith Paget**

Chief Executive, Caerphilly Local Health Board, Wales

**Dr Katherine Payne**

Health Economist, The North West Genetics Knowledge Park, The University of Manchester

**Dr Ann Richardson**

Independent Research Consultant

**Dr Stephen Saltissi**

Consultant Cardiologist, Royal Liverpool University Hospital

**Mr Mike Spencer**

General Manager, Clinical Support Services, Cardiff and Vale NHS Trust

**Dr Debbie Stephenson**

Head of HTA Strategy, Eli Lilly and Company

**Professor Andrew Stevens (Vice Chair)**

Professor of Public Health, University of Birmingham

**Dr Cathryn Thomas**

General Practitioner, & Associate Professor, Department of Primary Care & General Practice, University of Birmingham

**Simon Thomas**

Consultant Physician, General Medicine and Clinical Pharmacology, Newcastle Hospitals NHS Trust

**Dr Norman Vetter**

Reader, Department of Epidemiology, Statistics and Public Health, College of Medicine, University of Wales, Cardiff

**Professor Mary Watkins**

Professor of Nursing, University of Plymouth

**Dr Paul Watson**

Medical Director, Essex Strategic Health Authority

The following individuals, representing the National Collaborating Centre responsible for developing the Institute's clinical guideline related to this topic, attended the meeting to observe and to contribute as advisors to the Committee.

- Dr Adrian Harnett, Consultant in Clinical Oncology, Norfolk and Norwich University Hospital NHS Trust.
- James Smallwood, Medical Director, Hampshire and Isle of Wight Health Authority.

## **B. NICE project team**

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

### **Zoe Garrett**

Technical Lead, NICE project team

### **Alana Miller**

Project Manager, NICE project team

## Appendix B. Sources of evidence considered by the Committee

- A The following manufacturer/sponsor provided a submission for this appraisal.
- o Roche Products Ltd
- B The evidence review group report for this appraisal was prepared by the School of Health and Related Research (SchARR): Ward S, Pilgrim H, Hind D (May 2006). Trastuzumab for the treatment of primary breast cancer in HER2 positive women: a single technology appraisal.
- C The following individuals were selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups. They gave their expert personal view on trastuzumab by providing written evidence to the Committee.
- Professor Robert Coleman, President, British Oncological Association, nominated by the Royal College of Radiologists as a clinical specialist.
  - Dr Andrew Tutt, Clinical Oncologist, Guys and St Thomas' Hospital, nominated by Breakthrough Breast Cancer as a clinical specialist.
  - Emma Kearns, ECM website Stakeholder Manager, Department of Education and Skills, nominated by Breast Cancer Care as a patient expert.
  - Caroline Sharpe, Company Director, Osbon, nominated by Breakthrough Breast Cancer as a patient expert.

## Appendix C. List of organisations involved in this appraisal

The following organisations are consultees/commentators in this appraisal.

Consultees are also invited to appeal against the Final Appraisal Determination.

### I Professional/specialist and patient/carer groups:

- o Association of Cancer Physicians
- o Breakthrough Breast Cancer
- o Breast Cancer Care
- o British Association of Surgical Oncology
- o British Oncology Pharmacy Association (BOPA)
- o CancerBACUP
- o Cancer Research UK
- o Department of Health
- o Newbury and Community PCT
- o Royal College of General Practitioners
- o Royal College of Nursing
- o Royal College of Pathologists
- o Royal College of Physicians' Medical Oncology Joint Special Committee
- o Royal Pharmaceutical Society
- o Welsh Assembly Government

### II Commentator organisations (without the right of appeal)

- o British National Formulary
- o National Coordinating Centre for Health Technology Assessment (NCCHTA)
- o NHS Quality Improvement Scotland
- o National Cancer Research Institute
- o National Collaborating Centre for Cancer
- o School of Health & Related Research, University of Sheffield.