

# NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

## Final Appraisal Determination

### Gemcitabine for the treatment of metastatic breast cancer

#### 1 Guidance

- 1.1 Gemcitabine in combination with paclitaxel, within its licensed indication, is recommended as an option for the treatment of metastatic breast cancer only when docetaxel monotherapy or docetaxel plus capecitabine are also considered appropriate.

#### 2 The technology

- 2.1 Gemcitabine (Gemzar, Eli Lilly and Company Ltd) is an anticancer drug that belongs to a class of drugs known as antimetabolites. Gemcitabine in combination with paclitaxel has a UK marketing authorisation for the treatment of patients with metastatic breast cancer who have relapsed following adjuvant/neo-adjuvant chemotherapy. Prior chemotherapy should have included anthracyclines unless clinically contraindicated. For further information see the summary of product characteristics.
- 2.2 The side-effect profile of gemcitabine plus paclitaxel is similar to that of other chemotherapeutic agents. The most common haematological adverse effect reported is neutropenia and the most common non-haematological adverse effects reported include fatigue and diarrhoea. For full details of side effects and contraindications, see the summary of product characteristics.
- 2.3 The acquisition cost of gemcitabine is £32.55 for a 200 mg vial and £162.76 for a 1 g vial (excluding VAT; British national formulary, 51st edition). The recommended dosing regimen for gemcitabine plus paclitaxel is 175 mg/m<sup>2</sup>

paclitaxel administered on day 1 over 3 hours as an intravenous infusion, followed by 1250 mg/m<sup>2</sup> gemcitabine administered as a 30–60 minute infusion on days 1 and 8 of each 21 day treatment cycle. The cost per patient of adding gemcitabine to six treatment cycles of paclitaxel will be approximately £2346 excluding costs of administration. 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 gemcitabine and a review of this submission by the Evidence Review Group (ERG) (appendix B).

- 3.1 The manufacturer's submission approached the decision problem by comparing gemcitabine plus paclitaxel with licensed taxane-based regimens: paclitaxel, docetaxel monotherapy, and docetaxel plus capecitabine. The population consisted of people who had relapsed and developed metastatic breast cancer following anthracycline-based adjuvant or neo-adjuvant chemotherapy, or non-anthracycline-based chemotherapy where anthracyclines were contraindicated. The manufacturer stated that gemcitabine plus paclitaxel would be considered for people who are younger and fitter than the general population of patients with metastatic breast cancer, and who are considered suitable for taxane-based therapy. The patients for whom gemcitabine plus paclitaxel would be considered also require "a higher level of efficacy than would be achieved with a monotherapy regimen, without the toxicity usually associated with a combination regimen", for example because of visceral metastasis. The primary outcome measure considered was overall survival. Secondary outcome measures included time to documented progression of disease, progression-free survival, overall response rates, pain and analgesia, quality of life and incidence of adverse events.

- 3.2 The manufacturer's submission presented evidence on the clinical effectiveness of gemcitabine plus paclitaxel based on a single randomised controlled trial (RCT), the JHQG trial, which compared gemcitabine plus paclitaxel with paclitaxel monotherapy. Final analyses of the JHQG trial showed that, compared with the 263 people in the paclitaxel arm of the trial, the 266 people in the gemcitabine plus paclitaxel arm of the trial had greater median overall survival (18.6 months versus 15.8 months,  $p = 0.0489$ ; hazard ratio: 0.82, 95% confidence interval 0.67 to 1.00,  $p = 0.0495$ ) and time to documented progression of disease (5.4 months versus 3.5 months,  $p = 0.0013$ ; hazard ratio: 0.73, 95% confidence interval 0.61 to 0.89,  $p = 0.0015$ ). The final results of the JHQG trial have not yet been published in a peer-reviewed journal.
- 3.3 Evidence on cost effectiveness presented in the manufacturer's submission was based on a Markov state-transition model with a 3-year horizon, equivalent to the typical life expectancy of people diagnosed with metastatic breast cancer. A series of pairwise economic analyses comparing gemcitabine plus paclitaxel with docetaxel monotherapy, paclitaxel monotherapy and docetaxel plus capecitabine was presented by the manufacturer. All these analyses were based on an indirect comparison in which weighted absolute treatment outcomes (including survival data) were pooled from single arms of different trials in published literature. In order to compare gemcitabine plus paclitaxel with paclitaxel monotherapy, the median overall survival estimate for gemcitabine plus paclitaxel was taken from the RCT comparing gemcitabine plus paclitaxel with paclitaxel monotherapy. However, for paclitaxel monotherapy, the manufacturer did not use overall survival estimates from this comparative study, but instead used the average of the pooled, weighted absolute survival data from single arms of different studies.

- 3.4 The base-case analysis compared gemcitabine plus paclitaxel with docetaxel monotherapy and resulted in an incremental cost-effectiveness ratio (ICER) of £17,200 per quality-adjusted life year (QALY). A comparison of gemcitabine plus paclitaxel with paclitaxel monotherapy resulted in an ICER of £30,100 per QALY. A comparison of gemcitabine plus paclitaxel with docetaxel plus capecitabine resulted in an ICER of £23,200 per QALY. The manufacturer presented a scenario analysis for gemcitabine plus paclitaxel against docetaxel monotherapy where the price of non-proprietary paclitaxel is assumed to be 55% less than that of proprietary paclitaxel: the ICER in this case fell from £17,200 per QALY to £4700 per QALY.
- 3.5 The Evidence Review Group (ERG) reviewed the evidence submitted for clinical and cost effectiveness. The ERG judged that when only the results of the JHQQ trial were considered, the manufacturer's submission contained a reasonable estimate of the clinical effectiveness of gemcitabine plus paclitaxel when compared with paclitaxel monotherapy. It was noted that the overall survival benefits of gemcitabine plus paclitaxel may have been diluted by a number of patients in the paclitaxel arm of the trial receiving second-line treatments that included gemcitabine, docetaxel, vinorelbine and capecitabine. The use of second-line treatments was similar in both arms of the trial except for a four-fold greater use of gemcitabine in the paclitaxel arm.
- 3.6 The ERG reviewed the economic model and judged its structure to be reasonable and based on previous economic studies. The main drivers of cost effectiveness are the estimates of overall survival, the cost of paclitaxel, and the utilities assigned to the health states in the model. The ERG's main source of concern was the indirect comparison method used by the manufacturer to generate the survival estimates for the economic model, which involved pooling treatment outcome data from single arms of different trials. The ERG commented that the method used by the manufacturer ignored the fact that RCTs are designed to measure relative treatment effects.

The indirect comparison method used does not preserve the benefits of randomisation and it is at best equivalent to observational studies.

- 3.7 The ERG raised concerns about the comparability of the trials from which the data were pooled. In particular, the ERG highlighted underlying differences in the patient characteristics in the trials, notably the lines of prior therapies received. Finally, the ERG noted that the manufacturer's indirect comparison estimated median overall survival with paclitaxel monotherapy to be longer than with docetaxel monotherapy. This contradicts the results of a head-to-head trial in which patients randomised to docetaxel monotherapy had greater median overall survival than those randomised to paclitaxel monotherapy.
- 3.8 By using the treatment efficacy data from both arms of the RCT comparing gemcitabine plus paclitaxel with paclitaxel monotherapy instead of the pooled estimates from the manufacturer's indirect comparisons, the ERG estimated the ICER for a comparison between gemcitabine plus paclitaxel and paclitaxel monotherapy to be £42,800 per QALY. In an illustrative analysis, the ERG found that using relative treatment effects to estimate overall survival for docetaxel monotherapy resulted in an ICER of £45,800 per QALY for a comparison of gemcitabine plus paclitaxel against docetaxel monotherapy.
- 3.9 Full details of the evidence is in the manufacturer's submission and the ERG report, both of which are available from [www.nice.org.uk/page.aspx?o=260234](http://www.nice.org.uk/page.aspx?o=260234)

## **4 Consideration of the evidence**

- 4.1 The Appraisal Committee (appendix A) reviewed the data available on the clinical and cost effectiveness of gemcitabine for the treatment of metastatic breast cancer, having considered evidence (appendix B) on the nature of the condition and the value placed on the benefits of gemcitabine by people with

metastatic 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 current clinical practice in the treatment of metastatic breast cancer following relapse after anthracycline-based regimens in adjuvant and neo-adjuvant settings. The Committee heard from the clinical specialists that gemcitabine plus paclitaxel would be valued as an option in a group of patients who required a higher level of efficacy than would be achieved with a single agent taxane (for example in patients with visceral metastasis) and who were also considered fit enough to receive combination therapy. The Committee heard from the clinical specialists that gemcitabine plus paclitaxel would probably be used as an alternative option to the combination of docetaxel plus capecitabine because it is considered to be equally effective but less toxic. Finally, the Committee heard from the clinical specialists that because capecitabine is an important option in later lines of therapy for metastatic breast cancer, the use of docetaxel plus capecitabine as a first-line choice would reduce the possibility of using capecitabine in later lines of therapy. The patient representatives confirmed that for patients whose condition required an alternative to single agent taxanes, gemcitabine plus paclitaxel was a useful option because of its efficacy and low level of toxicity.

### **Clinical effectiveness**

- 4.3 The Committee considered the evidence on the clinical effectiveness of gemcitabine plus paclitaxel for the treatment of metastatic breast cancer. The Committee noted that the JHQQ trial is the only RCT comparing gemcitabine plus paclitaxel with paclitaxel monotherapy, and the final results of the trial have not yet been published in a peer-reviewed journal. The Committee considered the uncertainty surrounding the clinical effectiveness data relating to the borderline statistical significance of median overall survival, the fact that the 95% confidence interval for the hazard ratio for median overall survival

included 1.00, and the possibility that the four-fold greater use of gemcitabine as second-line treatment in the paclitaxel arm of the trial may have influenced the results. The Committee considered evidence from post hoc analyses of the JHQG trial provided by the manufacturer that showed that 95% confidence intervals of the hazard ratio for median overall survival did not include 1.00. The Committee was mindful that repeated post hoc statistical tests increase the likelihood of generating apparently statistically significant results, and agreed that the pre-planned primary analysis of median overall survival was the most reliable analysis of the JHQG trial. Based on the primary analysis of the JHQG trial, the Committee concluded that gemcitabine plus paclitaxel is likely to be more clinically effective than paclitaxel monotherapy, but recognised substantial uncertainty concerning the size of the treatment effect.

### **Cost effectiveness**

- 4.4 The Committee considered the evidence on the cost effectiveness of gemcitabine plus paclitaxel when compared with all relevant UK comparators as presented in the manufacturer's submission. The Committee noted that the manufacturer provided estimates of the cost effectiveness of gemcitabine plus paclitaxel versus paclitaxel monotherapy using only data from the indirect comparisons. The Committee also noted the ERG's view that using the actual data from the trial that directly compared gemcitabine plus paclitaxel with paclitaxel monotherapy provided an ICER of £42,800 per QALY.
- 4.5 The Committee understood that, given the lack of head-to-head trials, indirect comparison methods are necessary in order to compare gemcitabine plus paclitaxel with docetaxel monotherapy or docetaxel plus capecitabine. The Committee discussed the indirect comparisons method used by the manufacturer, and expressed concerns about the pooling of treatment outcome data from single arms of different trials. The Committee noted that recent medical statistical literature has concluded that the approach to indirect

comparisons used by the manufacturer is flawed and tends to produce inconsistencies between direct and indirect estimates of treatment effects. The Committee noted that a mixed treatment comparison meta-analysis that maintains the benefits of randomisation and requires a connected network of RCTs could have been carried out to indirectly compare all of the treatments simultaneously.

- 4.6 The Committee noted that the manufacturer's economic analysis suggested that the ICER for gemcitabine plus paclitaxel was lower when compared with docetaxel monotherapy than with paclitaxel monotherapy. The Committee noted that the survival estimates from the manufacturer's indirect comparisons appeared to contradict the results from a study that directly compared docetaxel monotherapy with paclitaxel monotherapy. The indirect comparison suggested that overall survival with paclitaxel monotherapy was superior to docetaxel monotherapy, but the clinical study suggested the opposite. Given that overall survival is a key driver of cost effectiveness in the manufacturer's economic model, the manufacturer's indirect survival estimates have the effect of producing cost-effectiveness ratios in favour of gemcitabine plus paclitaxel when compared with docetaxel monotherapy.
- 4.7 The Committee also discussed survival estimates calculated by the ERG, using an indirect comparison method that was based on relative treatment efficacy data that maintained the randomised structure of clinical trials. The Committee considered the ICER of £45,800 per QALY obtained using the ERG's indirect estimates for a comparison of gemcitabine plus paclitaxel with docetaxel monotherapy. Although the ERG's analyses were indicative and for illustrative purposes only, the ERG's indirect survival estimates were more consistent with, and closer to, the results from the head-to-head trial between docetaxel monotherapy and paclitaxel monotherapy. Furthermore, the Committee accepted that the manufacturer's indirect estimates were inconsistent with published evidence, and subject to substantial uncertainty.

- 4.8 The Committee noted that both the manufacturer and clinical experts positioned gemcitabine plus paclitaxel for the treatment of patients for whom combination chemotherapy would be most appropriate. The Committee discussed the clinical experts' view that docetaxel plus capecitabine was likely to be as clinically effective as gemcitabine plus paclitaxel but more toxic. The Committee concluded that the clinical evidence before it did not clearly indicate whether gemcitabine plus paclitaxel was more or less clinically effective than docetaxel plus capecitabine, but it was persuaded that docetaxel plus capecitabine was likely to be more toxic than gemcitabine plus paclitaxel. The Committee further concluded that gemcitabine plus paclitaxel was likely to be as clinically effective as docetaxel monotherapy. On this basis the Committee agreed that that gemcitabine plus paclitaxel could be a useful alternative when docetaxel monotherapy or docetaxel plus capecitabine were being considered in an individual patient. However, the Committee noted that the ERG had not provided an estimate of the ICER for a comparison between gemcitabine plus paclitaxel and docetaxel plus capecitabine. Taking into consideration the inconsistencies of the manufacturer's indirect estimates of treatment effects, the Committee concluded that the ICER presented in the manufacturer's submission for gemcitabine plus paclitaxel compared with docetaxel plus capecitabine was likely to be a substantial underestimate.
- 4.9 The Committee heard from the NHS Purchasing and Supply Agency (PASA) and Welsh Health Supplies (WHS) that the discounts on non-proprietary paclitaxel referred to in the manufacturer's submission are available throughout England and Wales. The Committee considered the impact and relevance of the discounts on non-proprietary paclitaxel for the economic analyses, and accepted that using the discounted non-proprietary paclitaxel prices could substantially lower the ICERs for gemcitabine plus paclitaxel (when compared with docetaxel monotherapy or docetaxel plus capecitabine) to levels of cost effectiveness previously considered to be an efficient use of NHS resources. The Committee considered that uncertainties remain over the

economic evidence presented by the manufacturer, but having had confirmation that discounts on non-proprietary paclitaxel are available throughout England and Wales, the Committee agreed that the ICERs for gemcitabine plus paclitaxel in comparison with docetaxel monotherapy and docetaxel plus capecitabine are likely to fall within acceptable levels of cost effectiveness. The Committee considered, however, that even with discounted non-proprietary paclitaxel, the ICER for a comparison of gemcitabine plus paclitaxel with paclitaxel would not fall within acceptable levels of cost effectiveness.

### **Summary of the considerations**

- 4.10 The Committee considered that the evidence presented by the manufacturer of the clinical and cost effectiveness of gemcitabine plus paclitaxel compared with the other licensed taxane-based treatments was subject to considerable uncertainties. The Committee concluded that the ERG's critique of the manufacturer's methods was valid and that the alternative approaches and resulting ICERs suggested by the ERG were more appropriate. The Committee accepted the confirmation from the NHS PASA and WHS of the availability of discounts on non-proprietary paclitaxel. The Committee considered the effect that the discounts would have on the economic analyses and results reported by both the manufacturer and the ERG. The Committee accepted that it was likely that the ICERs for gemcitabine plus paclitaxel compared with docetaxel monotherapy or docetaxel plus capecitabine would fall within acceptable levels of cost effectiveness. The Committee concluded gemcitabine plus paclitaxel, within its licensed indication, should be recommended as an option for the treatment of metastatic breast cancer in the NHS when docetaxel monotherapy or docetaxel plus capecitabine are considered appropriate.

## 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/TAXXX](http://www.nice.org.uk/TAXXX)).

## 6 Related guidance

- 6.1 NICE has issued the following related technology appraisals.
- Taxanes (docetaxel and paclitaxel) for the treatment of breast cancer. NICE technology appraisal 30 (September, 2001). Available from: [www.nice.org.uk/TA030](http://www.nice.org.uk/TA030)

- Trastuzumab for the treatment of advanced breast cancer. NICE technology appraisal 34 (March, 2002). Available from: [www.nice.org.uk/TA034](http://www.nice.org.uk/TA034)
- Vinorelbine for the treatment of advanced breast cancer. NICE technology appraisal 54 (June, 2005). Available from: [www.nice.org.uk/TA054](http://www.nice.org.uk/TA054)
- Capecitabine for the treatment of locally advanced and metastatic breast cancer. NICE technology appraisal 62 (May, 2003). Available from: [www.nice.org.uk/TA062](http://www.nice.org.uk/TA062)

6.2 NICE is in the process of producing the following clinical guideline.

- Breast cancer (early and advanced): diagnosis and treatment (publication expected July 2008)

## **7 Review of guidance**

7.1 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.

7.2 The guidance on this technology will be considered for review in January 2010.

David Barnett  
 Chair, Appraisal Committee  
 November 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 three times a month except in December, when there are no meetings. The Committee membership is split into three branches, each with a chair and vice chair. 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, Addenbrooke's Hospital, Cambridge

#### **Dr Tom Aslan**

General Practitioner, Stockwell, London

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**Professor David Barnett (Chair)**

Professor of Clinical Pharmacology, University of Leicester

**Mrs Elizabeth Brain**

Lay Member

**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 Rowan Hillson**

Consultant Physician, Diabeticare, The Hillingdon Hospital

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**Professor Philip Home (Vice Chair)**

Professor of Diabetes Medicine, University of Newcastle upon Tyne

**Dr Terry John**

General Practitioner, The Firs, London

**Professor Richard Lilford**

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

**Dr Simon Maxwell**

Senior Lecturer in Clinical Pharmacology and Honorary Consultant Physician,  
Queens Medical Research Institute

**Ms Judith Paget**

Chief Executive, Caerphilly Local Health Board, Wales

**Dr Ann Richardson**

Lay Member

**Mr Mike Spencer**

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

**Simon Thomas**

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

**Mr David Thomson**

Lay Member

**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

**B. Guideline representatives**

The following individual(s), representing the National Collaborating Centre responsible for developing the Institute's clinical guideline on this topic, were invited to attend the ACD meeting as observers and to contribute as advisers to the Committee.

- Dr Nicholas Murray, Guideline Development Group

## **C. 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), a technical advisor and a project manager.

### **Ebenezer Tetteh**

Technical Lead

### **Janet Robertson**

Technical Advisor

### **Alana Miller**

Project Manager

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

A The following manufacturer/sponsor provided a submission for this appraisal:

- Eli Lilly & Company Ltd

B The evidence review group (ERG) report for this appraisal was prepared by Southampton Health Technology Assessment Centre: J Jones, A Takeda, SC Tan, K Cooper, E Loveman, A Clegg, N Murray (July 2006). Gemcitabine for metastatic breast cancer.

C The following individuals were selected from clinical specialist and patient advocate nominations from the professional/specialist and patient/carer groups. They gave their expert personal views on gemcitabine plus paclitaxel by providing written and/or oral evidence to the Committee. They were also invited to comment on the Appraisal Consultation Document (ACD).

- Professor Steve Heys, Professor of Surgical Oncology, nominated by the British Association of Surgical Oncologists as a clinical specialist
- Dr Andreas Makris, Consultant Clinical Oncologist, nominated by the Royal College of Physicians as a clinical specialist
- Dr Mark Verrill, Consultant Medical Oncologist, nominated by the Royal College of Physicians as a clinical specialist
- Maria Leadbeater, Nurse Specialist Secondary Breast Cancer, nominated by Breast Cancer Care as a patient expert
- Anna Wood, Policy and Campaigns Manager, nominated by Breast Cancer Care 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:

- Association of Cancer Physicians
- Association of Surgeons of Great Britain and Ireland
- British Association of Surgical Oncology
- British Oncological Association
- British Oncology Pharmacy Association (BOPA)
- British Psychosocial Oncology Society (BPOS)
- Cancer Research UK
- Community Practitioners' & Health Visitors Association
- Medical Women's Federation
- Royal College of General Practitioners
- Royal College of Nursing
- Royal College of Pathologists
- Royal College of Physicians' Medical Oncology Joint Special Committee
- Royal College of Radiologists
- Royal College of Surgeons
- Royal Pharmaceutical Society
- Breakthrough Breast Cancer
- Breast Cancer Campaign
- Breast Cancer Care
- Cancer Voices
- Cancerbackup
- Long-term Medical Conditions Alliance
- Macmillan Cancer Relief

- Marie Curie Cancer Care
- National Cancer Alliance
- National Council for Palliative Care
- Tenovus Cancer Information Centre

II Commentator organisations (without the right of appeal):

- Board of Community Health Councils in Wales
- British National Formulary
- Medicines and Healthcare products Regulatory Agency (MHRA)
- National Public Health Service for Wales
- NHS Confederation
- NHS Purchasing and Supplies Agency
- NHS Quality Improvement Scotland
- Baxter Healthcare Ltd
- Bayer plc
- Bristol-Myers Squibb Pharmaceuticals Ltd
- Genus Pharmaceuticals
- GlaxoSmithKline
- Goldshield Pharmaceuticals Ltd
- Kyowa Hakko UK Ltd
- Mayne Pharma plc
- Medac UK
- Pfizer Ltd [Pharmacia]
- Pierre Fabre Ltd
- Roche Products Ltd
- Sanofi-Aventis
- Schering-Plough Ltd
- Wyeth Pharmaceuticals
- Cochrane Collaboration- Cochrane Breast Cancer Group

- Institute of Cancer Research
- MRC Clinical Trials Unit
- National Cancer Research Institute
- National Coordinating Centre for Health Technology Assessment
- Southampton Health Technology Assessment Centre
- National Collaborating Centre for Cancer