# NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

## Final appraisal determination

## Capecitabine for the treatment of advanced gastric cancer

This guidance was developed using the single technology appraisal (STA) process.

# 1 Guidance

1.1 Capecitabine in combination with a platinum-based regimen is recommended for the first-line treatment of inoperable advanced gastric cancer.

# 2 The technology

2.1 Capecitabine (Xeloda, Roche Products) is an orally administered pro-drug of fluorouracil. It is converted to fluorouracil by enzymes that are principally located in the liver and tumour tissue. This leads to a higher concentration of fluorouracil in tumour tissue than in normal tissues. Capecitabine has a UK marketing authorisation for the first-line treatment of advanced gastric cancer in combination with a platinum-based regimen.

2.2 According to the summary of product characteristics (SPC), contraindications include known dihydropyrimidine dehydrogenase deficiency, severe leucopenia, neutropenia or thrombocytopenia, severe hepatic impairment and severe renal impairment. The SPC states that capecitabine has been associated with hand–foot

syndrome, diarrhoea, neutropenia, peripheral neuropathy, headache and alopecia. For full details of side effects and contraindications, see the SPC.

2.3 Capecitabine is administered orally. The recommended dose of capecitabine is 625 mg/m$^2$ twice daily for 21 days if it is used as part of the epirubicin, cisplatin and capecitabine (ECX) regimen, or the epirubicin, oxaliplatin and capecitabine (EOX) regimen. If it is used as part of a capecitabine and cisplatin (CX) regimen, the recommended dose of capecitabine is 1000 mg/m$^2$ twice daily for 14 days in every 21 days. Treatment should be stopped if the disease gets worse or if there is intolerable toxicity. The cost of 60 150-mg tablets of capecitabine is £40.02 and the cost of 120 500-mg tablets is £265.55 (excluding VAT; Monthly Index of Medical Specialities [MIMS], March 2010). 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 capecitabine and a review of this submission by the Evidence Review Group (ERG; appendix B).

3.1 The manufacturer's submission considered the use of capecitabine with epirubicin plus cisplatin or oxaliplatin compared with fluorouracil with epirubicin plus cisplatin or oxaliplatin, and capecitabine plus cisplatin compared with fluorouracil plus cisplatin. The population was people with locally advanced (that is, the disease had spread to regional lymph nodes) or metastatic (that is, the disease had spread beyond the regional lymph nodes to other parts of the body) inoperable gastric cancer. This was in line with the scope, which restricted the population to people with inoperable advanced gastric cancer. The manufacturer reported details of two

phase III multicentre randomised controlled trials (REAL-2 and ML17032). These trials assessed the non-inferiority of capecitabine compared with fluorouracil for the treatment of advanced gastric cancer. REAL-2 compared ECX and EOX combinations with epirubicin/cisplatin/fluorouracil (ECF) and epirubicin/oxaliplatin/fluorouracil (EOF) combinations. ML17032 compared CX with cisplatin/fluorouracil (CF).

3.2 The REAL-2 trial was an open-label UK multicentre study that enrolled adults with advanced carcinoma of the oesophagus, oesophageal–gastric junction or stomach. People were included in the trial if they had locally advanced or metastatic adenocarcinoma, squamous cell carcinoma or undifferentiated carcinoma. In addition the primary tumour had to be classified as inoperable. People were randomised to receive capecitabine plus platinum-based chemotherapy regimens: ECX regimen (n = 241), ECF regimen (n = 249), EOX regimen (n = 239) or EOF regimen (n = 235). The doses were as specified in the individual SPCs of each drug. In all cases treatment was repeated every 3 weeks for 8 cycles in the absence of progressive disease or unacceptable toxicity. The primary endpoint was to determine non-inferiority of overall survival in people receiving capecitabine compared with those receiving fluorouracil, and non-inferiority of overall survival in people receiving oxaliplatin compared with those receiving cisplatin. The null hypothesis of non-inferiority of the capecitabine regimen was rejected if the upper limit of the 95% confidence interval (CI) around the hazard ratio (HR) for overall survival was more than 1.23.

3.3 The manufacturer reported that REAL-2 met the two primary non-inferiority endpoints, and that there was a trend towards improved survival in favour of both capecitabine over fluorouracil and oxaliplatin over cisplatin. The manufacturer also reported that the

trial showed non-inferiority in terms of overall survival for capecitabine; the HR adjusted for performance status, extent of disease and age was 0.89 (95% CI 0.77 to 1.02) in the per-protocol population. This was based on the comparison of ECF and EOF versus ECX and EOX. The manufacturer also reported that for the secondary endpoints, there was no significant difference in progression-free survival between the capecitabine and the fluorouracil arms or between the cisplatin and the oxaliplatin arms. There was minimal quality-of-life data reported in REAL-2 and there were no differences between the mean scores at baseline and 12 weeks between any of the groups on the General Health Status subscale of the European Organization for Research and Treatment of Cancer (EORTC)-30 questionnaire.

3.4 ML17032 was an open-label study that enrolled people with advanced gastric adenocarcinoma. Adults were included in the trial if they had histologically confirmed gastric adenocarcinoma with advanced and/or metastatic disease and at least one measurable lesion according to Response Evaluation Criteria in Solid Tumors (RECIST) that had not been irradiated and a Karnofsky performance status score of 70% or higher. People were randomised to receive cisplatin (80 mg/$m^2$ intravenously, day 1) plus fluorouracil (800 mg/$m^2$ intravenously, days 1–5 as a continuous infusion) (n = 156) or cisplatin (80 mg/$m^2$ intravenously, day 1) plus capecitabine (1000 mg/$m^2$ orally, twice daily, days 1–14) (n = 160). The primary endpoint was non-inferiority of progression-free survival. The null hypothesis of non-inferiority of the capecitabine regimen was rejected if the upper limit of the 95% CI around the HR for progression-free survival was more than 1.25.

3.5 In the per-protocol population, there was non-inferiority of progression-free survival in people receiving CX compared with those receiving CF (adjusted HR 0.85, 95% CI 0.65 to 1.11). The manufacturer reported that the results showed a trend towards improved progression-free survival with CX compared with CF in the unadjusted analysis. The median overall survival was 10.5 months for CX compared with 9.3 months for CF (HR 0.85, 95% CI 0.64 to1.13). It was also reported by the manufacturer that the trial demonstrated non-inferiority of capecitabine compared with fluorouracil for the secondary end-points of overall survival, response rate, mean time of response and duration of response. No quality of life data were collected in ML17032.

3.6 The manufacturer also reported a published meta-analysis that combined the individual data from 1318 people taking part in the REAL-2 and ML17032 trials. The aim of the meta-analysis was to test whether capecitabine was superior to fluorouracil within the double and triple combination chemotherapy regimens for people with advanced oesophago–gastric cancer. The primary endpoint was overall survival and the secondary endpoints were progression-free survival and response rate. The median overall survival for the intention-to-treat population was 285 days (95% CI 265 to 305 days) for people treated with fluorouracil (n = 664) and 322 days (95% CI 300 to 343 days) for people treated with capecitabine (n = 654). This resulted in an unadjusted HR of 0.87 (95% CI 0.77 to 0.98, p = 0.027) in favour of capecitabine. There was no evidence of any statistically significant heterogeneity of treatment effect according to baseline patient characteristics (such as age, disease site and histology). The meta-analysis reported that superiority of capecitabine over fluorouracil was maintained with multivariate analyses (adjusted HR 0.87, 95% CI 0.77 to 0.98, p = 0.02).The meta-analysis also reported a non statistically

significant trend towards improved progression-free survival in people receiving capecitabine (unadjusted HR 0.91, 95% CI 0.81 to 1.02, p = 0.093).

3.7 In REAL-2, grade 3 and 4 neutropenia was more common in the ECX arm compared with the ECF arm and there was an increased level of fatigue in the EOF arm compared with the EOX arm. Stomatitis occurred more frequently and with greater severity in the CF arm than in the CX arm in ML17032, while hand–foot syndrome was more common in the CX arm. The ML17032 trial also reported that adverse events leading to dose modification were more common in the CX arm (62%) compared with the CF arm (48%).

3.8 On the basis of equivalent clinical effectiveness, similar safety and improved patient convenience, a cost-minimisation model was developed to evaluate the costs for each regimen. The manufacturer reported that this captured all significant incremental direct costs relating to switching from fluorouracil-based therapies to capecitabine-based therapies. The model considered both the drug acquisition and drug administration costs for all the regimens evaluated. People entered the model at the start of treatment when they received either capecitabine or fluorouracil and left the model after 5.5 cycles (21 days per cycle), which was the time horizon of the model. The costs of treatment-related adverse events were not included. The overall tolerability profile of capecitabine was considered by the manufacturer to be similar and at least as good as fluorouracil. The manufacturer also stated that the adverse events associated with the method by which fluorouracil is administered, such as central-line complications, can be expensive to manage. This meant that the costs associated with the management of adverse events with capecitabine were unlikely to be higher than those associated with fluorouracil. Therefore, the

non-inclusion of adverse events costs in the model would be expected to favour fluorouracil.

3.9 The manufacturer stated that the economic evaluation of capecitabine was undertaken within its licensed indication for the first-line treatment of advanced gastric cancer in combination with a platinum-based regimen. There were three sets of analyses: a comparison of ECX with ECF, EOX with EOF, and CX with CF. A total of six regimens were therefore analysed in the cost-minimisation model. The dosages in each regimen were analysed according to the SPC for each treatment and no drug wastage was taken into account. The manufacturer also conducted some additional sensitivity analyses that included one-way sensitivity analyses, scenario analyses, a worst case scenario analysis and threshold analyses.

3.10 The base-case results included all the drug acquisition and administration costs for all the regimens considered in the submission. All capecitabine-based regimens were shown to be cost saving compared with equivalent fluorouracil-based regimens. The overall NHS cost saving for switching from ECF to ECX regimens was £1620. The overall NHS cost saving for switching from EOF to EOX regimens was £1572. For the double combination chemotherapy regimens the overall NHS saving of switching from CF to CX was £4210. All the results of the sensitivity and scenario analyses conducted by the manufacturer supported the base case and suggested that capecitabine-based regimens were cost saving compared with fluorouracil-based regimens.

3.11 The ERG considered that the clinical-effectiveness evidence presented by the manufacturer reflected the available relevant evidence. It noted that the ML17032 trial was underpowered since the trial had only 50% power to detect statistically significant non-

inferiority. The REAL-2 and the ML17032 trials used appropriate outcomes, but there were limited data on health-related quality of life. The ERG also noted that in clinical practice, fluorouracil and capecitabine would be administered in lower doses in the double combination chemotherapy regimen compared with the doses used in ML17032.

3.12 Overall, the ERG considered the manufacturer's approach to the economic evaluation reasonable and that the cost-minimisation analysis used in the submission was acceptable. The ERG stated that there was minimal change to the savings when many of the assumptions used were explored. The ERG pointed out that treatments cannot be considered to be exactly equivalent due to uncertainty in estimating their effectiveness. By conducting a cost-minimisation analysis, the manufacturer did not address the uncertainty around the estimates of efficacy. However, they performed a threshold analysis but the ERG noted that modelling a scenario in which fluorouracil was more effective was unlikely to be relevant to the determination of capecitabine's cost effectiveness. The ERG noted that adverse events had not been included in the cost-minimisation model because the manufacturer assumed that the costs associated with adverse event management were unlikely to be higher for capecitabine than fluorouracil. The ERG highlighted that rare adverse events may not have been identified because of the large sample sizes needed to detect these. Therefore, the ERG felt that some uncertainty remained about treatment-related adverse events associated with capecitabine and fluorouracil regimens. The ERG also noted that number of cycles used in the model did not represent the number used in UK clinical practice: the maximum number of cycles in clinical practice is usually six, but in REAL-2 the median (rather than the maximum) number of cycles received was six.

3.13 The ERG noted some additional areas of uncertainty. In the model, the manufacturer calculated capecitabine costs based on milligrams used. The ERG considered that in clinical practice, this would be rounded to match the available tablets. It also considered that in calculating fluorouracil costs, wastage had not been taken into account. The ERG noted that when calculating epirubicin, cisplatin and oxaliplatin costs, the manufacturer used an average of the NHS list prices. In practice, the NHS is likely to prefer the cheapest product. The ERG also considered that, in practice, the dose of capecitabine may be reduced by 25–50% because of toxicity. The ERG undertook exploratory analyses that took into account many of the above areas of uncertainty. In all analyses capecitabine was cost saving compared with fluorouracil.

3.14 Full details of all the evidence are in the manufacturer's submission and the ERG report, which are available from www.nice.org.uk/guidance/TAXXX

# 4 Consideration of the evidence

The Appraisal Committee reviewed the data available on the clinical and cost effectiveness of capecitabine, having considered evidence on the nature of gastric cancer and the value placed on the benefits of capecitabine by people with the condition, those who represent them, and clinical specialists. It also took into account the effective use of NHS resources.

## *Clinical effectiveness*

4.1 The Committee considered the clinical effectiveness of capecitabine for the treatment of advanced gastric cancer from the two open-label trials that assessed the non-inferiority of capecitabine compared with fluorouracil. The Committee noted that the results of the trials indicated that capecitabine was not inferior

to fluorouracil for overall survival (REAL-2 trial) and progression-free survival (ML17032 trial). There was also a trend to improved survival with capecitabine in the published meta-analysis of both trials. The Committee noted the ERG concerns that the ML17032 study was underpowered. The Committee also noted that with non-inferiority trials, it was possible for a treatment to achieve non-inferiority with a worse point estimate than the comparator treatment. Therefore, the Committee carefully considered the estimates from the trials and the published meta-analysis and their confidence intervals. The Committee agreed that the results of the studies showed a trend towards improved survival and concluded that capecitabine was probably at least as effective as intravenously administered fluorouracil.

4.2 The Committee noted that the REAL-2 trial was conducted in UK centres, although it included people with cancer involving the gastro–oesophageal junction and distal oesophagus as well as the stomach, and a small minority with squamous cell carcinoma rather than adenocarcinoma. However, the Committee accepted that the two trials were generalisable to people with advanced, inoperable gastric cancer in the UK. In addition, the Committee noted that the people in both trials were relatively young, with good performance status. The clinical specialists highlighted that even though the people in the trials were younger than the median age of death of people with gastric cancer, the trial population was representative of those in UK clinical practice who would be prescribed a chemotherapy regimen. Therefore the Committee concluded that the trials were sufficiently representative of UK practice.

4.3 The Committee considered current clinical practice for the first-line treatment of inoperable advanced gastric cancer. It heard about the experience of people receiving treatment and whether people

preferred oral treatment with capecitabine or intravenous treatment (via an infusion pump) with fluorouracil. The patient expert and clinical specialists explained that oral treatment allows for easier dose adjustment and less frequent visits to hospital, compared with an infusion pump that has to be replaced weekly. Oral treatment also offers an advantage for people in terms of carrying on with daily physical activities without the continuous presence of a pump. In addition, complications related to the presence of an indwelling venous line such as infection and line misplacement are avoided. The clinical specialists explained that the majority of people prefer oral treatment as long as there is no increase in adverse events.

4.4 The Committee considered whether there were issues related to equality to be taken into account in its considerations. It acknowledged that some people with inoperable advanced gastric cancer may not be able to swallow oral capecitabine tablets, because of difficulty with swallowing as a result of the cancer, or because of nausea. However the Committee noted that although capecitabine is preferred in most circumstances, fluorouracil remains an alternative where capecitabine is contraindicated or otherwise unsuitable. Therefore, it concluded that there were no specific issues relating to equality that needed to be taken into account.

4.5 The Committee then discussed hand–foot syndrome, which is a specific adverse event that occurs more frequently with capecitabine therapy than with intravenously administered fluorouracil. The clinical specialists noted that if reported early it can be successfully treated with emollient cream, vitamin B6 and temporary dose reduction. The Committee concluded that oral capecitabine therapy was the preferred first-line treatment option in most people able to tolerate it.

### *Cost effectiveness*

4.6 The Committee heard evidence on the cost effectiveness of capecitabine for the first-line treatment of inoperable advanced gastric cancer. It agreed that in this case the cost-minimisation analysis was an appropriate approach to the economic evaluation based on the clinical evidence that suggested that capecitabine was at least as effective as fluorouracil. The Committee recognised there were limited quality-of-life data but accepted that there was no reason to anticipate any major differences in quality of life between capecitabine-based and fluorouracil-based regimens.

4.7 The Committee noted that the model assumed that there were no significant differences in the incidence or severity of adverse events between capecitabine and fluorouracil regimens, and so the costs of treatment-related adverse events were not included in the analysis. The Committee agreed that based on the trial data this was acceptable. The Committee then discussed the length of the model. It agreed that the time horizon of 5.5 cycles was a reasonable assumption as this was the mean number of treatment cycles given in the REAL-2 trial and is reflective of UK clinical practice. The Committee concluded that the parameters used in the model were acceptable.

4.8 The Committee noted that the model showed that capecitabine-based regimens were cost saving compared with fluorouracil-based regimens. The Committee heard that the ERG had noted some areas of uncertainty and had undertaken exploratory analyses to assess these. However, in all these analyses, capecitabine was still likely to be cost saving compared with fluorouracil. The Committee therefore agreed that capecitabine would be a cost-effective use of NHS resources. The Committee concluded that capecitabine, in combination with a platinum-based regimen, should be

recommended for the first-line treatment of inoperable advanced gastric cancer.

## Summary of the Appraisal Committee's key conclusions

| TAXXX (STA) | Appraisal title: Capecitabine for the treatment of advanced gastric cancer | FAD section |
|---|---|---|
| **Key conclusion** | | |
| The Committee concluded that capecitabine, in combination with a platinum-based regimen, should be recommended for the first-line treatment of inoperable advanced gastric cancer. | | 4.8 |
| **Current practice** | | |
| Clinical need | The patient expert and clinical specialists explained that oral treatment allows for easier dose adjustment and less frequent visits to the hospital, compared with an infusion pump that has to be replaced weekly. In addition, complications related to the presence of an indwelling venous line such as infection and line misplacement are avoided. | 4.3 |
| Availability of alternative treatments | The Committee considered current clinical practice for the first-line treatment of inoperable advanced gastric cancer. It heard about the experience of people receiving treatment and whether people preferred oral treatment with capecitabine or intravenous treatment (via an infusion pump) with fluorouracil. The clinical specialists explained that the majority of people prefer oral treatment as long as there is no increase in adverse events. | 4.3 |
| The position of the treatment in the pathway of care for the condition | Capecitabine has a UK marketing authorisation for the first-line treatment of advanced gastric cancer in combination with a platinum-based regimen. | 2.1 |
| **The technology** | | |
| Proposed benefits of the technology from the manufacturer, clinician and patient perspective | The patient expert and clinical specialists explained that oral treatment allows for easier dose adjustment and less frequent visits to the hospital, compared with an infusion pump that has to be replaced weekly. Oral treatment also offers an advantage for people in terms of carrying on with daily physical activities without the continuous presence of a pump. | 4.3 |
| Distinguishing features of the technology | Capecitabine is an orally administered pro-drug of fluorouracil. | 2.1 |
| Adverse effects | The Committee discussed hand–foot syndrome, which is a specific adverse event that occurs more frequently with capecitabine therapy than with intravenously administered fluorouracil. The clinical specialists noted that if reported early it can be successfully treated with emollient cream, vitamin B6 and temporary dose reduction. | 4.5 |
| **Evidence for clinical effectiveness** | | |
| Availability and nature of evidence | The Committee considered the clinical effectiveness of capecitabine for the treatment of advanced gastric cancer from two open-label trials that assessed the non-inferiority of capecitabine compared with fluorouracil. | 4.1 |

| | | |
|---|---|---|
| Quality of the evidence | The Committee carefully considered the estimates from the trials and the published meta-analysis and their confidence intervals, noting the ERG concerns that one of the studies was underpowered. The Committee agreed that the results of the studies showed a trend towards improved survival and concluded that capecitabine was probably at least as effective as intravenously administered fluorouracil. | 4.1 |
| Relevance to general clinical practice in the NHS | The Committee accepted that the two trials were generalisable to people with advanced, inoperable gastric cancer in the UK. In addition, the Committee noted that the people in both trials were relatively young, with good performance status. The clinical specialists highlighted that even though the people in the trials were younger than the median age of death of people with gastric cancer, the trial population was representative of those in UK clinical practice who would be prescribed a chemotherapy regimen. Therefore the Committee concluded that trials were sufficiently representative of UK clinical practice. | 4.2 |
| Uncertainties generated by the evidence | The Committee noted the ERG concerns that the ML17032 study was underpowered. The Committee also noted that with non-inferiority trials, it was possible for a treatment to achieve non-inferiority with a worse point estimate than the comparator treatment. Therefore, the Committee carefully considered the estimates from the trials and the published meta-analysis and their confidence intervals. | 4.1 |
| Are there any clinically relevant subgroups for which there is evidence of differential effectiveness? | None | |
| **Evidence for cost effectiveness** | | |
| Availability and nature of evidence | The Committee heard evidence on the cost effectiveness of capecitabine for the first-line treatment of inoperable advanced gastric cancer. It agreed that in this case the cost-minimisation analysis was an appropriate approach to the economic evaluation based on the clinical evidence that suggested that capecitabine was at least as effective as fluorouracil. | 4.6 |
| Uncertainties around and plausibility of assumptions and inputs in the economic model | The Committee noted that the model assumed that there were no significant differences in the incidence or severity of adverse events between capecitabine and fluorouracil regimens, and so the costs of treatment-related adverse events were not included in the analysis. The Committee agreed that based on the trial data this was acceptable. The Committee then discussed the length of the model. It agreed that the time horizon of 5.5 cycles was a reasonable assumption as this was the mean number of treatment cycles given in the REAL-2 trial and is reflective of UK clinical practice. The Committee concluded that the parameters used in the model were acceptable. | 4.7 |
| Incorporation of health-related quality-of-life benefits and utility values | The Committee recognised there were limited quality-of-life data but accepted that there was no reason to anticipate any major differences in the quality of life between capecitabine-based and fluorouracil-based regimens. | 4.6 |
| Are there specific groups of people for whom the technology is particularly cost effective? | None | |

| | | |
|---|---|---|
| Most likely cost-effectiveness estimate (given as an ICER) | The Committee noted that the model showed that there were likely to be cost savings with capecitabine-based regimens compared with fluorouracil-based regimens. | 4.8 |
| **Additional factors taken into account** | | |
| Patient access scheme (Pharmaceutical Price Regulation Programme) | No patient access scheme was submitted for the technology being appraised. | |
| End of life considerations (supplementary advice on end of life) | Because the most plausible ICER was not more than £30,000 per QALY gained, the supplementary advice was not relevant. | |
| Equalities considerations, social value judgement | The Committee considered whether there were issues related to equality to be taken into account in its considerations. It acknowledged that some people with inoperable advanced gastric cancer may not be able to swallow oral capecitabine tablets because of difficulty with swallowing as a result of the cancer, or because of nausea. However the Committee agreed noted that although capecitabine is preferred in most circumstances, fluorouracil remains an alternative where capecitabine is contraindicated or otherwise unsuitable. Therefore, it concluded that there were no specific issues relating to equality that needed to be taken into account. | 4.4 |

# 5 Implementation

5.1 The Secretary of State and the Welsh Assembly Minister for Health and Social Services have issued directions to the NHS on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends use of a drug or treatment, or other technology, the NHS must provide funding and resources for it within 3 months of the guidance being published. If the Department of Health issues a variation to the 3-month funding direction, details will be available on the NICE website. The NHS is not required to fund treatments that are not recommended by NICE.

5.2 NICE has developed tools to help organisations put this guidance into practice (listed below). These are available on our website (www.nice.org.uk/guidance/TAXXX). [NICE to amend list as needed at time of publication]

- Slides highlighting key messages for local discussion.
- Costing report and costing template to estimate the savings and costs associated with implementation.
- Implementation advice on how to put the guidance into practice and national initiatives that support this locally.
- A costing statement explaining the resource impact of this guidance.
- Audit support for monitoring local practice.

# 6 Related NICE guidance

**Under development**

NICE is developing the following guidance (details available from www.nice.org.uk):

- Trastuzumab for the treatment of HER2 positive advanced gastric cancer. NICE technology appraisal (publication expected November 2010)

# 7 Review of guidance

7.1 The guidance on this technology will be considered for review in May 2013. The Guidance Executive will decide whether the technology should be reviewed based on information gathered by NICE, and in consultation with consultees and commentators.

Jane Adam
Chair, Appraisal Committee
May 2010

# Appendix A: Appraisal Committee members, guideline representatives and NICE project team

## *A Appraisal Committee members*

The Appraisal Committees are standing advisory committees of NICE. 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. There are four Appraisal Committees, each with a chair and vice chair. Each Appraisal Committee meets once a month, except in December when there are no meetings. Each Committee considers its own list of technologies, and ongoing topics are not moved between Committees.

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 (Chair)**

Department of Diagnostic Radiology, St George's Hospital

**Professor A E Ades**

Professor of Public Health Science, Department of Community Based Medicine, University of Bristol

**Elizabeth Brain**

Lay Member

**Dr Fiona Duncan**

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

**Dr Paul Ewings**

Statistician, Taunton & Somerset NHS Trust, Taunton

**John Goulston**

Chief Executive, Barking, Havering and Redbridge Hospitals NHS Trust

**Adrian Griffin**

VP Strategic Affairs, LifeScan, Johnson & Johnson

**Dr Alec Miners**

Lecturer in Health Economics, London School of Hygiene and Tropical Medicine

**Dr Ann Richardson**

Lay Member

**Angela Schofield**

Chairman, Bournemouth and Poole Teaching PCT

**David Thomson**

Lay Member

**William Turner**

Consultant Urologist, Addenbrooke's Hospital

**Professor Karl Claxton**

Professor of Health Economics, University of York

**Dr David Newsham**

Lecturer (Orthoptics), University of Liverpool

**Professor Iain Squire**

Consultant Physician, University Hospitals of Leicester

**Dr James Moon**

Consultant Cardiologist and Senior Lecturer, University College London Hospital (UCLH) and UCL

**Dr Peter Heywood**

Consultant Neurologist, Frenchay Hospital

**Dr Ian Lewin**

Consultant Endocrinologist, North Devon District Hospital

**Dr Louise Longworth**

Reader in Health Economics, HERG, Brunel University

**Christopher Earl**

Surgical Care Practitioner, Renal Transplant Unit, Manchester Royal Infirmary

**Dr Anthony S Wierzbicki**

Consultant in Metabolic Medicine / Chemical Pathology, Guy's and St Thomas' Hospitals NHS Trust

**Professor Jonathan Grigg**

Professor of Paediatric Respiratory and Environmental Medicine, Barts and the London School of Medicine and Dentistry, Queen Mary University London

**Dr John Watkins**

Clinical Senior Lecturer / Consultant in Public Health Medicine, Cardiff University and National Public Health Service Wales

**Dr Olivia Wu**

Reader in Health Economics, University of Glasgow

**Dr Paul Robinson**

Medical Director, Merck Sharp & Dohme

## *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), a technical adviser and a project manager.

**Raphael Yugi and Sally Doss**

Technical Leads

**Rebecca Trowman**

Technical Adviser

**Bijal Joshi**

Project Manager

# Appendix B: Sources of evidence considered by the Committee

A The Evidence Review Group (ERG) report for this appraisal was prepared by Centre for Reviews and Dissemination, University of York:

- Norman G, Soares M, Peura P, et al., Capecitabine for the treatment of advanced gastric cancer, February 2010

B The following organisations accepted the invitation to participate in this appraisal as consultees and commentators. They were invited to comment on the draft scope. Organisations listed in I were also invited to make written submissions. Organisations listed in II gave their expert views on capecitabine by providing a written statement to the Committee. Organisations listed in I, II and III have the opportunity to appeal against the final appraisal determination.

I Manufacturer/sponsor:

- Roche Products (capecitabine)

II Professional/specialist and patient/carer groups:

- Cancer Research UK
- Macmillan Cancer Support
- Royal College of Nursing
- Royal College of Physicians, Medical Oncology Joint Special Committee

III Other consultees:

- Department of Health
- Welsh Assembly Government

IV Commentator organisations (did not provide written evidence and without the right of appeal):

- Department of Health, Social Services and Public Safety for Northern Ireland
- National Institute for Health Research Health Technology Assessment Programme
- NHS Centre for Reviews & Dissemination and Centre for Health Economics – York
- NHS Quality Improvement Scotland

C The following individuals were selected from clinical specialist and patient expert nominations from the non-manufacturer/sponsor consultees and commentators. They gave their expert personal view on capecitabine by providing oral evidence to the Committee.

- Dr Alicia Okines, Clinical Research Fellow, nominated by The Royal College of Physicians – clinical specialist
- Dr Anne L Thomas, Senior Lecturer in Medical Oncology, nominated by The Royal College of Physicians – clinical specialist
- Abrar Hussain-Qureshi, nominated by Macmillan Cancer Support – patient expert

D Representatives from the following manufacturer/sponsor attended Committee Meetings. They contributed only when asked by the Committee chair to clarify specific issues and comment on factual accuracy.

- Roche Products