NICE National Institute for Health and Care Excellence

NICE guidance

Cetuximab for the treatment of locally advanced squamous cell cancer of the head and neck

Technology appraisal guidance
Published: 25 June 2008

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Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1 Recommendations

1.1 Cetuximab in combination with radiotherapy is recommended as a treatment option only for patients with locally advanced squamous cell cancer of the head and neck whose Karnofsky performance-status score is 90% or greater and for whom all forms of platinum-based chemoradiotherapy treatment are contraindicated.

1.2 Patients currently receiving cetuximab in combination with radiotherapy for the treatment of locally advanced squamous cell cancer of the head and neck who do not meet the criteria outlined in section 1.1 should have the option to continue therapy until they and their clinicians consider it appropriate to stop.

1.3 When using Karnofsky performance-status score, clinicians should be mindful of the need to secure equality of access to treatment for patients with disabilities. Clinicians should bear in mind that people with disabilities may have difficulties with activities of daily living that are unrelated to their prognosis with respect to cancer of the head and neck. In such cases, clinicians should make appropriate judgements of performance status taking into account the person's usual functional capacity and requirement for assistance with activities of daily living.

2 The technology

2.1 Cetuximab (Erbitux, Merck Pharmaceuticals) is a chimeric immunoglobulin G monoclonal antibody that competes for epidermal growth factor receptor (EGFR) binding sites on the external surface of the cell membrane. Binding of cetuximab to EGFR prevents activation of tyrosine kinase within cells, eventually resulting in apoptosis. Cetuximab, in combination with radiotherapy, is licensed for the treatment of patients with locally advanced squamous cell cancer of the head and neck. For further information, see the summary of product characteristics (SPC).

2.2 The most common side effects of cetuximab are mild or moderate infusion-related reactions such as fever, chills, nausea, vomiting, headache, dizziness or dyspnoea that occur soon after the first cetuximab infusion. Skin reactions develop in more than 80% of patients and mainly present as an acne-like rash or, less frequently, as pruritus, dry skin, desquamation, hypertrichosis or nail disorders (for example, paronychia). The majority of skin reactions develop within the first 3 weeks of therapy. For full details of side effects and contraindications, see the SPC.

2.3 The acquisition cost of cetuximab is £136.50 for a 5-mg/ml, 20-ml vial (excluding VAT; BNF, edition 55). The initial dose is 400 mg/m^2 body surface area. Subsequent weekly doses are 250 mg/m^2 each. A course of treatment can range from 2 to 8 weeks. Assuming a body surface area range of 1.6 m^2 to 1.8 m^2, the drug cost of a course of treatment comprising 2 to 8 cycles is £4,778 to £5,870. Costs may vary in different settings because of negotiated procurement discounts.

3 The manufacturer's submission

The Appraisal Committee considered evidence submitted by the manufacturer of cetuximab and a review of this submission by the Evidence Review Group (ERG). The Committee further considered evidence submitted by consultees and commentators requested by NICE after the appeal.

3.1 The manufacturer's submission approached the decision problem by comparing cetuximab plus radiotherapy with radiotherapy alone. The manufacturer specified that the population under consideration consisted of people with locally advanced squamous cell cancer of the head and neck for whom chemotherapy is considered inappropriate but for whom radiotherapy is suitable. The outcome measures specified in the decision problem were duration of locoregional control, overall survival, progression-free survival and safety.

3.2 The manufacturer's submission presented evidence on the clinical effectiveness of cetuximab plus radiotherapy based on a single randomised controlled trial (RCT; the Bonner trial) that compared cetuximab plus radiotherapy with radiotherapy alone in people with stage III or IV non-metastatic squamous cell cancer of the oropharynx, hypopharynx or larynx. Criteria for eligibility included medical suitability for definitive radiotherapy, a Karnofsky performance-status score of at least 60%, and normal haematopoietic, hepatic and renal function. Patients were not included in the trial if they had undergone surgery or had previously received radiotherapy for head and neck cancer. The primary outcome measure was the duration of control of locoregional disease. The secondary endpoints were overall survival, progression-free survival, response rate and safety.

3.3 Final analyses of the trial showed that the 211 people in the cetuximab plus radiotherapy arm had a longer median duration of locoregional control than the 213 people in the radiotherapy-alone arm (24.4 versus 14.9 months, p=0.005, hazard ratio [HR] 0.68, 95% confidence interval [CI] 0.52 to 0.89) and greater median overall survival (49.0 versus 29.3 months, p=0.03, HR 0.74, 95% CI 0.57 to 0.97).

3.4 The manufacturer's submission presented a de novo economic analysis that

compared cetuximab plus radiotherapy with radiotherapy alone. The model used individual patient data from the RCT to estimate costs and health effects during the trial period for each patient. When trial observations were censored, the model extrapolated costs and health effects.

3.5 The base-case analysis compared cetuximab plus radiotherapy with radiotherapy alone and resulted in an incremental cost-effectiveness ratio (ICER) of £6,400 per quality-adjusted life year (QALY) gained. The manufacturer undertook a univariate sensitivity analysis, which demonstrated that the model was not sensitive to change when assessing the effect of uncertainty in a variety of inputs. Relatively large variability was observed when the timeframe of the analysis changed from a lifetime to the period of the trial follow-up, resulting in an ICER of £20,000 per QALY gained.

3.6 The ERG reviewed the evidence on clinical and cost effectiveness submitted by the manufacturer. The ERG judged that the 1 trial included in the manufacturer's submission was well conducted and that the results for the primary endpoints appeared robust. However, the ERG noted that the majority of patients in the trial population had a good performance status (Karnofsky performance-status score ranged from 60% to 100% but was most commonly 90%), and chemotherapy would be expected to be suitable for them. Therefore, the population of the trial did not match the population described in the decision problem, that is, patients for whom chemoradiotherapy is considered inappropriate. Furthermore, there are differences between the radiotherapy regimens used in the trial and those most commonly used in UK clinical practice.

3.7 The ERG reviewed the economic model and identified a number of concerns. The most important of these was that the only RCT informing the economic analysis (the Bonner trial) did not match the patient population specified in the manufacturer's decision problem. The manufacturer provided a set of possible criteria for defining patients for whom chemoradiotherapy is inappropriate, based on discussions with a small number of oncologists. In addition, the manufacturer was asked to provide information on the number of patients in the trial for whom chemoradiotherapy was considered inappropriate. However, the manufacturer stated that it was unable to provide analyses based on these criteria as the RCT was not designed or statistically powered to assess subgroups of patients for whom chemoradiotherapy may be considered inappropriate.

3.8 In addition, the ERG identified a series of issues and uncertainties about the methods for extrapolation of the trial data, assessment of health-related quality of life (HRQoL), and estimation of resource use and costs. The ERG concluded that the methods used were probably appropriate but was unable to determine, in the majority of cases, the likely influence of using alternative methods on the results of the economic model. However, the ERG concluded that altering the method of extrapolation would be unlikely to cause the ICER to increase to above £20,000.

3.9 The ERG undertook additional work to examine the robustness of the base-case results to the assumptions made in the manufacturer's cost-effectiveness model about HRQoL, resource use and cost. The ERG concluded that any inaccuracies would have to be very large to have a material effect on the conclusions of the manufacturer's cost-effectiveness analysis.

3.10 The ERG felt that although the economic analyses undertaken by the manufacturer demonstrated that cetuximab in combination with radiotherapy was cost effective compared with radiotherapy alone under a broad range of different assumptions (assuming a threshold of £20,000 per QALY), the cost-effectiveness estimates might not be directly applicable to the population specified in the manufacturer's decision problem (that is, patients for whom chemoradiotherapy is considered inappropriate). This was because the clinical study on which the economic analysis was based included a substantial proportion of patients for whom chemoradiotherapy would be considered suitable.

3.11 Following an appeal hearing, the Appeal Panel requested that the manufacturer provide subgroup survival data (derived from the Bonner trial) for each of the separate Karnofsky performance-status score subgroups (Karnofsky performance-status scores of 100%, 90%, 80%, 70% and less than 70%). The manufacturer stated that the number of patients in some of the subgroups was small (numbers ranged from 12 to 91), and this should be taken into consideration when interpreting these data. For patients with Karnofsky performance-status scores of 100% and 90%, the survival HRs were in favour of cetuximab plus radiotherapy over radiotherapy alone (HR 0.61, 95% CI 0.28 to 1.31, and HR 0.58, 95% CI 0.39 to 0.88 for Karnofsky performance-status scores of 100% and 90%, respectively). For patients with Karnofsky performance-status scores of 80%, 70% and less than 70%, the survival HRs were in favour of radiotherapy alone

over cetuximab plus radiotherapy (HR 1.11, 95% CI 0.69 to 1.77; HR 1.22, 95% CI 0.53 to 2.78; and HR 3.41, 95% CI 0.65 to 17.7, respectively).

3.12 The manufacturer was further asked by the Appeal Panel to provide cost-effectiveness estimates for the subgroup analyses described in section 3.11. The analyses were conducted using the manufacturer's original cost-effectiveness model. The manufacturer's analysis gave ICERs for cetuximab in combination with radiotherapy versus radiotherapy alone of £13,151 and £4,467 per additional QALY gained for patients with Karnofsky performance-status scores of 100% and 90%, respectively. For patients with Karnofsky performance-status scores of 70%, radiotherapy alone dominated cetuximab in combination with radiotherapy (that is, radiotherapy alone was more effective in terms of QALYs gained and was less expensive). For patients with Karnofsky performance-status scores of 80% and less than 70%, the manufacturer reported ICERs for cetuximab in combination with radiotherapy versus radiotherapy alone of £58,200 and £37,000 per additional QALY gained, respectively.

3.13 Following the appeal hearing, NICE invited the manufacturer and consultees and commentators to provide or highlight further evidence on the efficacy of carboplatin monotherapy in combination with radiotherapy, and on the safety or toxicity of carboplatin with fluorouracil and radiotherapy in patients with locally advanced squamous cell cancer of the head and neck. The manufacturer undertook a literature review and identified 22 studies on the efficacy of carboplatin monotherapy and radiotherapy, none of which were phase III studies or meta-analyses. Six of the 22 studies reported median overall survival estimates, which ranged from 6.7 months to 30 months. The manufacturer considered the median overall survival estimate of 30 months reported by Jeremic and colleagues (n=53) to be the most robust. The manufacturer further identified 9 published studies on the efficacy and safety of carboplatin with fluorouracil and radiotherapy, of which 3 were phase III trials. The phase III studies reported median overall survival estimates of 23 months, 20 months and 19 months (n=113, 109 and 64, respectively), and haematological toxicities (grade 3 or 4 acute toxicities) of 23% and 29.5% (n=113 and 64, respectively). Consultees highlighted that there was little published evidence on the efficacy of carboplatin-based chemoradiotherapy compared with cisplatin-based chemoradiotherapy or with radiotherapy alone, but that carboplatin-based chemoradiotherapy can be used as a treatment for patients for whom cisplatin-

based chemoradiotherapy is not an option.

3.14 Full details of all the evidence are in the manufacturer's submission and the ERG report.

4 Consideration of the evidence

4.1 The Appraisal Committee reviewed the data available on the clinical and cost effectiveness of cetuximab, having considered evidence on the nature of the condition and the value placed on the benefits of cetuximab by people with locally advanced squamous cell cancer of the head and neck, those who represent them, and clinical specialists. 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 described in the manufacturer's submission was reasonable, but noted that the population specified excluded people for whom chemotherapy is suitable. Therefore the decision problem did not reflect the entire population of people with locally advanced squamous cell cancer of the head and neck for whom cetuximab might be considered as a treatment option according to its licensed indication.

4.3 The Committee considered current UK clinical practice in the treatment of locally advanced squamous cell cancer of the head and neck. It heard from the clinical specialist who attended the meeting that chemoradiotherapy is the standard care for patients with stage lll and IV squamous cell cancer of the head and neck. However, there are patients for whom chemoradiotherapy is considered inappropriate (for example, patients with co-existing medical conditions and poor performance status). Chemoradiotherapy carries a high risk of adverse effects and patients should be willing and fit enough to be treated. The clinical specialist and patient experts were of the opinion that for patients whose condition required an alternative to chemoradiotherapy, cetuximab plus radiotherapy was a useful option because of its relatively low toxicity profile compared with chemotherapy.

4.4 The Committee heard from the clinical specialist that there is considerable variation in clinical practice across the UK. There are no clear definitions or criteria for patients for whom chemoradiotherapy is considered inappropriate, and there is variation in the selection of initial treatment modality (surgery or chemoradiotherapy), radiation dose intensities and the means of delivery of chemotherapy. More intensive radiotherapy regimens require suitable infrastructure and patients may need to attend hospital all day (which some are

unable to do).

4.5 The Committee considered the evidence on the clinical effectiveness of cetuximab in combination with radiotherapy for the treatment of locally advanced squamous cell cancer of the head and neck. It noted that there was only 1 relevant RCT that compared cetuximab plus radiotherapy with radiotherapy alone in people with non-resected disease (the Bonner trial). The Committee noted that the trial had started at a time when radiotherapy rather than chemoradiotherapy was the standard treatment. The Committee accepted that cetuximab with radiotherapy had been shown to be more effective than radiotherapy alone in the population represented in the trial.

4.6 The Committee noted that there were no trials that compared cetuximab plus radiotherapy directly with any platinum-based chemoradiotherapy. The Committee understood that chemoradiotherapy is considered to be standard treatment for patients unless there are reasons to contraindicate its use, and that cetuximab plus radiotherapy might have advantages over chemoradiotherapy in terms of reduced toxicity. However, the Committee was not presented with any evidence comparing cetuximab plus radiotherapy with chemoradiotherapy on which an estimate of the clinical and cost effectiveness of cetuximab in combination with radiotherapy could be based. Therefore the Committee was unable to make any recommendations on its use as an alternative to chemoradiotherapy.

4.7 The Committee considered the use of cetuximab in combination with radiotherapy in the population specified in the manufacturer's decision problem, that is, the subgroup of patients for whom chemoradiotherapy was considered to be unsuitable by the manufacturer. The Committee noted that the population in the relevant RCT was relatively fit: more than two-thirds had a Karnofsky performance-status score of 90% or above and all had normal haematopoietic, hepatic and renal function. The manufacturer was unable to provide information on the number of patients in the RCT for whom chemoradiotherapy would have been inappropriate, or on the effectiveness of cetuximab plus radiotherapy in this subgroup.

4.8 The Committee considered that patients with lower Karnofsky performance-status scores would form most, if not all, of the population for whom

chemoradiotherapy would be considered inappropriate in clinical practice. The Committee discussed the subgroup analyses of the median overall survival data according to Karnofsky performance-status scores provided by the manufacturer and reported in the 'European public assessment report' published by the European Medicines Agency. Although recognising the difficulties in interpreting the subgroup analyses, the Committee noted that no clinical benefit had been demonstrated for cetuximab in combination with radiotherapy in patients with a Karnofsky performance-status score of 80% or less. The Committee concluded that given the absence of clinical benefit (albeit with wide confidence intervals) it could not make the subgroup of patients with Karnofsky performance-status scores of 80% or less the basis for a positive recommendation to use cetuximab in combination with radiotherapy. Indeed, the Committee noted that the 'European public assessment report' stated that the 'overall impression of all subgroup analyses is that the add-on effect of cetuximab tends to be small or absent irrespective of outcome measure in patients with poor prognosis (estimated from median overall survival)'.

4.9 The Committee then considered patients with a Karnofsky performance-status score of 90% or greater and explored situations in which chemoradiotherapy might be unsuitable for them. The Committee reviewed the criteria proposed by consultees for identifying patients with good performance status and for whom cisplatin-based chemoradiotherapy would be inappropriate. It noted from consultees that some patients who are unable to tolerate the nephrotoxicity, ototoxicity and fluid overload from cisplatin-based chemoradiotherapy prefer carboplatin-based chemoradiotherapy. The Committee was made aware by consultees that although carboplatin does not have a UK marketing authorisation for the treatment of locally advanced squamous cell cancer of the head and neck, carboplatin-based combination regimens have been studied in this condition and are sometimes used to treat this condition in UK clinical practice. However, the Committee also heard that carboplatin-based regimens are associated with haematological adverse effects, particularly myelosuppression. The Committee concluded that although carboplatin-based chemoradiotherapy is a treatment option for some patients for whom cisplatin-based chemoradiotherapy is contraindicated, it was possible that there are some patients with good Karnofsky performance-status scores for whom any type of platinum-based chemoradiotherapy is contraindicated. The Committee accepted that the results presented for patients with Karnofsky performance-status scores of 90% or

greater indicated that cetuximab in combination with radiotherapy would be more effective than radiotherapy alone in this subgroup.

4.10 The Committee considered the ICER presented by the manufacturer in its original submission and the ERG's original comments. The Committee noted that the ICER of £6,400 for cetuximab in combination with radiotherapy versus radiotherapy alone was robust to the main sensitivity analyses. The Committee considered the ICERs presented by the manufacturer for each Karnofsky performance-status score subgroup separately. It noted that the ICERs for patients with a score of 90% or greater were favourable and similar to the overall estimate in the base case. The Committee was persuaded that although there was uncertainty about the number of patients within the subgroups who would have met the criteria to receive chemoradiotherapy, cetuximab in combination with radiotherapy is cost effective for patients with a Karnofsky performance-status score of 90% or greater and for whom chemoradiotherapy is not an option. However, for those with a Karnofsky performance-status score of 80% or less, the HR for survival did not favour cetuximab and therefore the ICERs were unfavourable. The Committee therefore was unable to recommend cetuximab for people with low performance status.

Summary of the considerations

4.11 The Committee concluded that cetuximab in combination with radiotherapy is clinically and cost effective in patients with locally advanced squamous cell cancer of the head and neck who have a Karnofsky performance-status score of 90% or greater and for whom platinum-based chemoradiotherapy treatment is contraindicated.

5 Implementation

5.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation within 3 months of its date of publication.

5.2 Chapter 2 of Appraisal and funding of cancer drugs from July 2016 (including the new Cancer Drugs Fund) – A new deal for patients, taxpayers and industry states that for those drugs with a draft recommendation for routine commissioning, interim funding will be available (from the overall Cancer Drugs Fund budget) from the point of marketing authorisation, or from release of positive draft guidance, whichever is later. Interim funding will end 90 days after positive final guidance is published (or 30 days in the case of drugs with an Early Access to Medicines Scheme designation or cost comparison evaluation), at which point funding will switch to routine commissioning budgets. The NHS England Cancer Drugs Fund list provides up-to-date information on all cancer treatments recommended by NICE since 2016. This includes whether they have received a marketing authorisation and been launched in the UK.

5.3 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal guidance recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final draft guidance.

5.4 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has locally advanced squamous cell cancer of the head and neck and the healthcare professional responsible for their care thinks that cetuximab is the right treatment, it should be available for use, in line with NICE's recommendations.

6 Recommendations for further research

6.1 A clinical trial on radiation therapy and cisplatin with or without cetuximab in patients with stage III or stage IV head and neck cancer (RTOG-0522) is currently recruiting patients.

6.2 The Committee recommends further research on the following:

- Cetuximab in combination with radiotherapy compared with radiotherapy alone in patients with low Karnofsky performance-status scores.
- Cetuximab in combination with radiotherapy compared with chemoradiotherapy in patients with high Karnofsky performance-status scores.

7 Appraisal Committee members and NICE project team

Appraisal Committee members

The Appraisal Committee is a standing advisory committee of NICE. 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 3 times a month except in December, when there are no meetings. The Committee membership is split into 3 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.

Professor David Barnett
Professor of Clinical Pharmacology, University of Leicester

Dr David W Black
Director of Public Health, Derbyshire County PCT

Mr Brian Buckley
Chairman, Incontact

Dr Carol Campbell
Senior Lecturer, University of Teesside

Professor Mike Campbell
Professor of Medical Statistics, University of Sheffield

Professor David Chadwick
Professor of Neurology, Liverpool University

Dr Peter Clarke
Consultant Medical Oncologist, Clatterbridge Centre for Oncology, Merseyside

MsJude Cohen
Manager of Resources & Administration, United Kingdom Council for Psychotherapy (UKCP)

Dr Christine Davey
Senior Researcher, North Yorkshire Alliance Research and Development Unit

Dr Mike Davies
Consultant Physician, Manchester Royal Infirmary

Mr Richard Devereaux-Phillips
Public Affairs Manager, Medtronic

Dr Rachel A Elliott
Lord Trent Professor of Medicines and Health, University of Nottingham

Mrs Eleanor Grey
Lay member

Dr Dyfrig Hughes
Senior Research Fellow in Pharmacoeconomics, Centre for the Economics of Health and Policy in Health, University of Wales

Dr Catherine Jackson
Clinical Lecturer in Primary Care Medicine, Alyth Health Centre

Dr Peter Jackson
Clinical Pharmacologist, University of Sheffield

Professor Peter Jones
Pro Vice Chancellor for Research & Enterprise, Professor of Statistics, Keele University

Ms Rachel Lewis
Practice Development Facilitator, Manchester PCT

Damien Longson
Consultant in Liaison Psychiatry, North Manchester General Hospital

Professor Jonathan Michaels
Professor of Vascular Surgery, University of Sheffield

Dr Eugene Milne
Deputy Medical Director, North East Strategic Health Authority

Dr Simon Mitchell
Consultant Neonatal Paediatrician, St Mary's Hospital, Manchester

Dr Richard Alexander Nakielny
Consultant Radiologist, Royal Hallamshire Hospital, Sheffield

Dr Katherine Payne
Health Economics Research Fellow, University of Manchester

Dr Martin J Price
Head of Outcomes Research, Janssen-Cilag

Dr Philip Rutledge
GP and Consultant in Medicines Management, NHS Lothian

Mr Miles Scott
Chief Executive, Bradford Teaching Hospitals NHS Foundation Trust

Professor Mark Sculpher
Professor of Health Economics, University of York

Professor Andrew Stevens
Chair of Appraisal Committee C

Dr Cathryn Thomas
GP and Associate Professor, University of Birmingham

Mr William Turner
Consultant Urologist, Addenbrookes Hospital, Cambridge

NICE project team

Each technology appraisal is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

Nicola Hay
Technical Lead

Janet Robertson
Technical Adviser

Chris Feinmann
Project Manager

8 Sources of evidence considered by the Committee

The Evidence Review Group (ERG) report for this appraisal was prepared by the Centre for Health Economics, University of York and NHS Northern and Yorkshire Regional Drug and Therapeutics Centre, Newcastle:

- Griffin S et al. Cetuximab for the treatment of locally advanced squamous cell carcinoma of the head and neck, September 2006.

The following organisations accepted the invitation to participate in this appraisal. They were invited to comment on the draft scope, the ERG report and the appraisal consultation document (ACD). The manufacturer or sponsor was also invited to make written submissions. Professional or specialist, and patient or carer groups gave their expert views on cetuximab by providing a written statement to the Committee. The manufacturer or sponsor, professional or specialist, and patient or carer groups, and commentator organisations (without the right of appeal) were requested to submit further evidence as a result of the appeal decision. The manufacturer or sponsor, and professional or specialist, and patient or carer groups have the opportunity to appeal against the final appraisal determination.

Manufacturer or sponsor:

- Merck Pharmaceuticals UK

Professional, specialist and patient or carer groups:

- British Association of Head and Neck Oncologists
- British Association of Head and Neck Oncology Nurses
- British Association of Oral and Maxillofacial Surgeons
- Cancer Networks Pharmacists Forum (BOPA)
- Cancer Research UK
- Cancerbackup

- Department of Health
- Get A-Head
- Let's Face it
- Mouth Cancer Foundation
- National Association of Laryngectomee Clubs
- Royal College of General Practitioners
- Royal College of Nursing
- Royal College of Paediatrics and Child Health
- Royal College of Pathologists
- Royal College of Physicians' Medical Oncology Joint Special Committee
- Royal College of Radiologists
- Royal Pharmaceutical Society
- Sheffield South West PCT
- Welsh Assembly Government

Commentator organisations (without the right of appeal):

- British National Formulary
- Centre for Health Economics, University of York and the Regional Drug and Therapeutics Centre, Newcastle
- Department of Health, Social Services and Public Safety for Northern Ireland
- King's College Hospital Maxillofacial Unit – The Head and Neck Oncology Group
- Medical Research Council (MRC) Clinical Trials Unit
- National Collaborating Centre for Cancer
- National Coordinating Centre for Health Technology Assessment

- NHS Quality Improvement

The following individuals were selected from clinical specialist and patient advocate nominations from the non-manufacturer or sponsor consultees and commentators. They gave their expert personal view on cetuximab by attending the initial Committee discussion and providing written evidence to the Committee. They were also invited to comment on the ACD.

- Dr Nick Slevin, Consultant Clinical Oncologist, Christie Hospital NHS Trust, nominated by the Royal College of Radiologists – clinical specialist
- Dr Kevin Harrington, Mayo Clinic College of Medicine, nominated by the Royal College of Radiologists – clinical specialist (written statement only)
- Ms Brenda Brady, nominated by the Mouth Cancer Foundation – patient expert
- Mrs Jean Fraser, nominated by the National Association of Laryngectomee Clubs – patient expert

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