NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Appraisal consultation document

Cetuximab for the treatment of recurrent and/or metastatic squamous cell cancer of the head and neck

The Department of Health has asked the National Institute for Health and Clinical Excellence (NICE or the Institute) to conduct a single technology appraisal (STA) of cetuximab for the treatment of recurrent and/or metastatic squamous cell cancer of the head and neck and provide guidance on its use to the NHS in England and Wales. The Appraisal Committee has had its first meeting to consider both the evidence submitted by the manufacturer and the views put forward by non-manufacturer consultees and commentators, and by the clinical specialist and patient expert representatives nominated for this appraisal by non-manufacturer consultees and commentators. The Committee has developed preliminary recommendations on the use of cetuximab for the treatment of recurrent and/or metastatic squamous cell cancer of the head and neck.

This document has been prepared for consultation with the formal consultees. It summarises the evidence and views that have been considered and sets out the preliminary recommendations developed by the Committee. The Institute is now inviting comments from the formal consultees in the appraisal process (the consultees for this appraisal are listed on the NICE website, www.nice.org.uk). This document should be read in conjunction with the evidence base for this appraisal (the evaluation report) which is available from www.nice.org.uk

Note that this document does not constitute the Institute's formal guidance on this technology. The recommendations made in section 1 are preliminary and may change after consultation.

The process the Institute will follow after the consultation period is summarised below. For further details, see the 'Guide to the single technology appraisal process' (this document is available on the Institute's website, www.nice.org.uk).

- The Appraisal Committee will meet again to consider the original evidence and this appraisal consultation document in the light of the views of the formal consultees.
- At that meeting, the Committee will also consider comments made on the document by people who are not formal consultees in the appraisal process.

- After considering feedback from the consultation process, the Committee will prepare the final appraisal determination (FAD) and submit it to the Institute.
- Subject to any appeal by consultees, the FAD may be used as the basis for the Institute's guidance on the use of the appraised technology in the NHS in England and Wales.

The key dates for this appraisal are:

Closing date for comments: 19 February 2009

Second Appraisal Committee meeting: 3 March 2009

Details of membership of the Appraisal Committee are given in appendix A, and a list of the sources of evidence used in the preparation of this document is given in appendix B.

Note that this document does not constitute the Institute's formal guidance on this technology. The recommendations made in section 1 are preliminary and may change after consultation.

1 Appraisal Committee's preliminary recommendations

1.1 Cetuximab in combination with platinum-based chemotherapy is not recommended for the treatment of recurrent and/or metastatic squamous cell cancer of the head and neck.

1.2 People currently receiving cetuximab in combination with platinum-based chemotherapy for the treatment of recurrent and/or metastatic squamous cell cancer of the head and neck should have the option to continue treatment until they and their clinician consider it appropriate to stop.

2 The technology

2.1 Cetuximab (Erbitux, Merck Serono) is a recombinant monoclonal antibody that blocks the human epidermal growth factor receptor (EGFR) and therefore inhibits the proliferation of cells that depend on EGFR activation for growth. Cetuximab is licensed for the treatment of patients with squamous cell cancer of the head and neck (SCCHN) in combination with platinum-based chemotherapy for recurrent and/or metastatic disease.

2.2 One common adverse effect of cetuximab treatment is the development of skin reactions, which occur 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 treatment. The summary of product characteristics (SPC) notes that if a patient experiences a severe skin reaction, cetuximab treatment must be interrupted, with treatment being resumed only when the reaction resolves to the extent that it affects less than 50% of the surface area of the skin. Other common adverse effects of cetuximab treatment include mild or moderate infusion-related reactions such as fever, chills, nausea, vomiting, headache, dizziness or dyspnoea that occur soon after the first cetuximab infusion. Treatment with cetuximab in combination with platinum-based chemotherapy may increase the frequency of severe leukopenia or severe neutropenia, and may lead to a higher rate of infectious complications such as febrile neutropenia, pneumonia and sepsis compared with platinum-based chemotherapy alone. 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; 'British national formulary' [BNF] edition 56). The initial dose is 400 mg/m^2 body surface area (BSA). Subsequent weekly doses are 250 mg/m^2 each. Cetuximab is used in combination with platinum-based chemotherapy followed by cetuximab as maintenance therapy until disease progression. Assuming that vials are not shared among patients, an average person with a BSA of 1.75 m^2 would receive seven vials per loading dose and five vials per maintenance dose, equating to a cost of £955.50 for the loading dose and £682.50 for each maintenance dose. Patients in the key clinical trial received cetuximab for approximately 18 weeks equating to an average total drug acquisition cost of £13,241 per patient. 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 cetuximab and a review of this submission by the Evidence Review Group (ERG; appendix B).

3.1 In the submission, the manufacturer compared a regimen of cetuximab plus cisplatin or carboplatin plus fluorouracil with cisplatin or carboplatin and fluorouracil in the first-line treatment of recurrent and/or metastatic SCCHN.

3.2 The main evidence on the efficacy of cetuximab in the manufacturer's submission was derived from one randomised controlled trial (RCT). The EXTREME trial (N = 442) was a multicentre, open-label RCT which compared cetuximab plus cisplatin or carboplatin and fluorouracil (cetuximab plus chemotherapy) with cisplatin or carboplatin and fluorouracil alone (chemotherapy alone). The primary outcome was overall survival time. Secondary outcome measures were progression-free survival; best overall response to therapy; disease control rate; time to treatment failure; and duration of response and quality of life (QoL).

3.3 The participants in the trial were patients with recurrent and/or metastatic SCCHN for whom local therapy was not suitable and who had a Karnofsky performance status (KPS) score of 70 or more. The planned treatment duration was until there was demonstration of progressive disease, or occurrence of unacceptable toxicity.

3.4 The EXTREME trial showed a statistically significant increase in median overall survival for cetuximab plus chemotherapy compared with chemotherapy alone (10.1 months and 7.4 months,

respectively; adjusted hazard ratio [HR] 0.797; 95% confidence interval [CI] 0.644 to 0.986, p = 0.036). There were also statistically significant increases in other secondary outcome measures for cetuximab plus chemotherapy compared with chemotherapy alone: progression-free survival (HR 0.538, p < 0.001); best overall response rate (odds ratio [OR] 2.326, p < 0.001); disease control rate (OR 2.881, p < 0.001); time to treatment failure (HR 0.59, p < 0.001). There was no statistically significant difference in the duration of response between the cetuximab plus chemotherapy and chemotherapy only groups (HR 0.76, p = 0.21).

3.5 The manufacturer presented a number of predefined subgroup analyses. The clinical subgroups included: age, KPS score, platinum regimen, previous treatment, primary tumour site, tumour grade, baseline QoL score and percentage EGFR-detectable cells. For overall survival, most subgroups were shown to benefit from cetuximab plus chemotherapy. The beneficial effect of adding cetuximab to chemotherapy was most marked in the group with primary tumours located in the oral cavity (HR 0.42, 95% CI 0.25 to 0.67).

3.6 QoL was assessed in the EXTREME trial using two related assessment tools: European Organisation for Research and Treatment of Cancer QoL questionnaire (EORTC QLQ) C30 (version 3) and EORTC QLQ-H&N35. The small proportion of patients whose disease responded at 12 months prevented any meaningful statistical analysis. In addition, another type of questionnaire was used only in the UK (EQ-5D). No analyses were carried out on these data due to the very small number of patients and responses available (12 assessments from 7 patients who completed questionnaires). The proportion of evaluable questionnaires for EORTC QLQ-C30 and QLQ-H&N35 was

considered by the manufacturer to be low (61% in the cetuximab plus chemotherapy group and 58% in the chemotherapy alone group). On the EORTC QLQ-C30 social functioning scale, no statistically significant differences were observed between the two treatment groups. Results of the QLQ-H&N35 questionnaire showed that, in general, the scores for the cetuximab plus chemotherapy group were not significantly worse than for the chemotherapy alone group. Some significant differences in favour of the cetuximab plus chemotherapy group were observed at cycle 3 for measures of pain, swallowing, speech problems and social eating. However, these differences were not apparent at month 6.

3.7 The incidence of most adverse events was similar in both groups, indicating that the addition of cetuximab to platinum-based chemotherapy did not significantly increase treatment toxicity. The exceptions to this were rash, acne, acneiform dermatitis, dry skin and anorexia which occurred more frequently (a 10% or greater difference) in the cetuximab plus chemotherapy group than in the chemotherapy alone group. Acneiform dermatitis and acne were reported only for the cetuximab plus chemotherapy group. Most of the more severe adverse events (grade 3 or 4), including haematological toxicities, occurred with similar frequencies in both treatment groups.

3.8 The manufacturer developed a two-arm state-transition Markov model to evaluate the cost effectiveness of cetuximab plus platinum-based chemotherapy compared with platinum-based chemotherapy alone. The clinical data used in the economic evaluation were generated from the EXTREME study. Although the economic evaluation was trial-based, there was a modelling component to allow extrapolation of health effects beyond the period of the study (24 months). Utilities were based on the EORTC

QLQ-30 data collected in the trial which were converted into EQ-5D scores using a cross walk algorithm originally developed for pancreatic cancer. Disutilities associated with adverse events were not accounted for separately. The patient's response to the EORTC QLQ-30 global questionnaire was assumed to capture the impact of adverse events on the patient's health-related QoL.

3.9 The categories of costs used in the economic model included: chemotherapy drugs (cetuximab, cisplatin, carboplatin and fluorouracil), drug administration, treatment of adverse events, palliative-intent chemotherapy drugs, palliative-intent surgery and palliative-intent radiology. Information on healthcare resources other than drug use and frequency of chemotherapy regimens, surgery and radiotherapy were not collected in the EXTREME study. The manufacturer therefore estimated the cost of these resources from the literature and key opinion leaders treating SCCHN.

3.10 The results of the base-case scenario for cetuximab plus platinum-based chemotherapy compared with platinum-based chemotherapy alone gave an incremental cost-effectiveness ratio (ICER) of £121,367 per quality-adjusted life year (QALY) gained.

3.11 In addition to the base-case scenario, the manufacturer also presented ICERs for the oropharynx, oral cavity, metastatic disease and recurrent disease subgroups. The ICERs presented were as follows:

- oropharynx and oral cavity, ICER of £105,069 per QALY gained
- oropharynx and oral cavity with KPS of 90 or more, ICER of £97,702 per QALY gained
- oropharynx, ICER of £250,597 per QALY gained

- oropharynx with KPS of 90 or more, ICER of £309,735 per QALY gained
- oral cavity, ICER of £63,927 per QALY gained
- oral cavity with KPS of 90 or more, ICER of £54,791 per QALY gained
- metastatic disease including recurrent disease, ICER of £562,849 per QALY gained
- metastatic disease excluding recurrent disease, dominated
- recurrent disease, ICER of £87,099 per QALY gained.

3.12 The ERG considered there to be a number of limitations with the evidence in the manufacturer's submission.

- The manufacturer submitted clinical evidence to support the use of cetuximab plus platinum-based chemotherapy for the first-line treatment of patients with recurrent and/or metastatic SCCHN, although neither the scope issued by NICE nor the licensed indication restricts the use of cetuximab to first-line treatment for this group of patients.
- Patients in the EXTREME trial may be younger and fitter (indicated by very high KPS scores) than patients with recurrent and/or metastatic SCCHN in the UK.
- There was concern that no evidence was provided by the manufacturer to support the use of cetuximab plus platinum-based chemotherapy in patients with recurrent and/or metastatic SCCHN who were not cetuximab-naive.
- The ERG highlighted that for several subgroups, including metastatic disease, there appeared to be no survival benefit from cetuximab plus platinum-based chemotherapy, although only the subgroup for tumour location showed a statistically significant interaction with treatment.

3.13 The ERG considered the economic model submitted by the manufacturer to be implemented to a generally high standard. However, the ERG identified a number of potential issues related to the manufacturer's economic submission, which were considered to compromise the validity of the model results. These included:

- the appropriateness of creating an economic model for this appraisal, since there was only one set of clinical trial results showing mortality in the follow-up period, covering 75–80% of enrolled patients
- the appropriateness of Weibull modelling for all patient groups. The ERG stated that it could not fully explore the appropriateness and reliability of the parametric survival projection models as the manufacturer chose not to provide all the requested information
- the absence of a mid-cycle correction
- uncertainty surrounding the health-related QoL data reported in the clinical trials and the estimates employed in the model
- the BSA value used, which does not take account of BSA differences among patients, including those due to gender
- an inconsistent price base for unit costs
- the exclusion of important parameters from the univariate sensitivity analysis (estimated overall survival time and the effect of inter-patient dosing variability on treatment costs) and probabilistic sensitivity analysis (uncertainty in the assumed value of the mean BSA that was used in the calculation of treatment costs).

3.14 The ERG considered that it was likely that at least some of the subgroups were too small to yield reliable projection models, casting doubt on the credibility of the cost-effectiveness results for those subgroups.

3.15 The ERG undertook exploratory analysis using alternative assumptions and parameters in the economic model. The key amendments made by the ERG were:

- the inclusion of a mid-cycle correction on the submitted base-case results
- to replace the projection modelling of costs and outcomes used in the base case with a comparison of the costs and outcomes at 24 months (end of follow-up period in the EXTREME trial)
- to use combined estimates of mean utility values throughout the analysis
- to replace the fixed mean BSA value (1.7 m^2) used in the manufacturer's model with a mean BSA of 1.83 m^2 (based on results of a UK audit study, weighted for the gender balance in the EXTREME trial)
- to re-analyse the unit costs used in the manufacturer's model by using a more consistent price base for costs. The ERG used the following sources: NHS reference costs for 2006/07 for inpatient, outpatient and investigations; PSSRU 2007 for primary care costs; BNF 56 (2008) for drug costs and Blood Transfusion Service prices for 2007/08, adjusted to 2006/07 prices assuming 4% inflation for transfusions.

3.16 The combined effects of the ERG's exploratory analysis on the original base case resulted in ICERs of £166,307 and £208,266 per QALY gained when based on a lifetime and a 24-month time horizon, respectively. The ERG stated that the most influential changes to cost arose from the recalculation of drug doses by BSA, which was partially offset by the introduction of a mid-cycle correction. The use of an overall pre-progression utility value in place of treatment-specific values was the main alteration to outcomes.

3.17 The ERG also carried out exploratory analysis to determine the effect of its model amendments on all the patient subgroups. In all cases the results of the analyses indicated that cetuximab plus chemotherapy was less cost effective with the ERG model and parameter corrections and/or amendments than when originally submitted by the manufacturer.

3.18 The ERG undertook threshold analysis to determine the cost for a vial of cetuximab that would generate an ICER below £30,000 per QALY gained. The ERG stated that it appears that the use of cetuximab plus chemotherapy may not be cost effective at any price. The ERG reported that there are three contributory processes influencing this result.

- Since cetuximab requires more frequent administration than chemotherapy, it incurs additional infusion costs twice every cycle, regardless of the price charged for the drug.
- The trial protocol requires that patients whose disease responds should continue receiving cetuximab until disease progression occurs, incurring greater drug and administration costs.
- Because cetuximab plus chemotherapy is associated with better survival, patients experience a longer period during which they are eligible to gain benefit from other follow-on treatments and palliative care, all of which involve additional NHS costs.

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

4 Consideration of the evidence

4.1 The Appraisal Committee reviewed the data available on the clinical and cost effectiveness of cetuximab for the treatment of recurrent and/or metastatic SCCHN, having considered evidence on the nature of the condition and the value placed on the benefits of cetuximab by people with recurrent and/or metastatic SCCHN, 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 reviewed the evidence available on the clinical effectiveness of cetuximab as presented in the manufacturer's submission and the ERG report. It noted that there was only one relevant RCT that compared cetuximab plus platinum-based chemotherapy with chemotherapy alone in patients with recurrent and/or metastatic SCCHN (the EXTREME trial). The Committee noted that few of the patients included in the clinical trial were from the UK although many were from other European countries. The Committee was also aware of the ERG's concern that the patients in the trial appeared younger and fitter, on the basis of higher KPS scores, than those patients presenting in the UK and therefore there was some uncertainty whether similar benefits from cetuximab would be replicated for patients with this condition in the UK. Additionally the Committee heard from the clinical specialists that most patients presenting with recurrent and/or metastatic SCCHN in the UK were older and had poorer general health than those recruited to the trial; however, those patients in whom platinum-based chemotherapy would be considered appropriate are more likely to be of a similar age and performance status to those represented in the EXTREME trial. Overall the Committee

accepted the evidence from the clinical specialists that the results of the EXTREME trial would be applicable to the UK population.

4.3 The Committee discussed the reported results from the clinical trial. It noted that the manufacturer had presented results for the total population in the trial and for a number of pre-planned subgroups. The Committee noted the statistically significant improvement in overall survival associated with cetuximab in the total population represented in the trial. The Committee was aware that in the subgroup analyses, only tumour location showed a significant interaction with treatment, suggesting greater effectiveness in tumours in the oral cavity. The Committee heard from the clinical specialists that patients with tumours located in the oral cavity have a relatively favourable prognosis compared with the average prognosis for recurrent and/or metastatic SCCHN, but the specialists were not aware of any biological reason for cetuximab to be more clinically effective in tumours located in the oral cavity. The Committee accepted that the trial demonstrated the efficacy of cetuximab plus platinum-based chemotherapy in patients with recurrent and/or metastatic SCCHN, but it was not persuaded that the evidence supported using a greater estimate of relative clinical effectiveness in patients with tumours located in the oral cavity.

4.4 The Committee discussed the adverse effects of cetuximab treatment. The Committee noted that the incidence of severe adverse events in the cetuximab plus platinum-based chemotherapy group and the platinum-based chemotherapy only group were broadly similar with the exception of acne and acneiform dermatitis, which were reported only for the cetuximab plus platinum-based chemotherapy group. The clinical specialists and a patient expert advised the Committee that the adverse events reported for the trial were consistent with those seen in

clinical practice where cetuximab had been used for locally advanced SCCHN and colorectal cancer.

4.5 The Committee discussed the cost effectiveness of cetuximab plus platinum-based chemotherapy compared with platinum-based chemotherapy alone. The Committee was aware that the ICERs presented by the manufacturer for the base-case and subgroup analyses were substantially higher than those normally considered to be an acceptable use of NHS resources (see sections 3.10 and 3.11). In addition, the Committee was mindful of the concerns raised by the ERG in relation to the extrapolation of the trial results that was necessary to estimate survival in the economic model, and the uncertainty about the number of patients available for analysis in each of the pre-planned subgroups. The Committee noted the exploratory analyses undertaken by the ERG using alternative assumptions and parameters in the economic model (see section 3.16). The Committee concluded that there remained considerable uncertainty around the results of the manufacturer's analyses and that it was plausible that the true cost-effectiveness estimate for cetuximab plus platinum-based chemotherapy would be even higher than that presented by the manufacturer.

4.6 The Committee considered supplementary advice from the Institute, to be taken into account when appraising treatments which may be life-extending for patients with short life expectancy, and which are licensed for indications affecting small numbers of patients with incurable illnesses. For this advice to be applied, all the following criteria must be met.

- The treatment is indicated for patients with a short life expectancy, normally less than 24 months.

- There is sufficient evidence to indicate that the treatment offers an extension to life, normally of at least an additional 3 months, compared with current NHS treatment.
- No alternative treatment with comparable benefits is available through the NHS.
- The treatment is licensed, or otherwise indicated, for small patient populations.
- In addition, when taking these into account the Committee must be persuaded that the estimates of the extension to life are robust and the assumptions used in the reference case economic modelling are plausible, objective and robust.

4.7 On this basis the Committee understood that it is estimated that about 3000 people per year are diagnosed with recurrent and/or metastatic SCCHN, but the Committee heard from the clinical specialists that cetuximab plus platinum-based chemotherapy would be appropriate for only a small proportion of these (those who have disease that is unsuitable for local treatment and are well enough to receive platinum-based chemotherapy). The Committee observed that the trial data suggest that cetuximab plus platinum-based chemotherapy extends survival relative to platinum-based chemotherapy alone. However, it noted that the estimate of life years gained from the addition of cetuximab to chemotherapy was 0.187 which equates to an average of 68 days. The Committee therefore did not consider that the magnitude of this benefit was in keeping with the supplementary advice for consideration of life-extending, end-of-life treatments.

4.8 The Committee concluded that cetuximab for recurrent and/or metastatic SCCHN could not be recommended as a cost-effective

use of NHS resources. The Committee noted that some people may be currently receiving cetuximab in combination with platinum-based chemotherapy for this indication and recommended that these people should have the option to continue treatment until they and their clinician consider it appropriate to stop.

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 that 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). [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 which support this locally.
- Audit support for monitoring local practice.

6 Related NICE guidance

Published

- Cetuximab for the treatment of locally advanced squamous cell cancer of the head and neck. NICE technology appraisal guidance 145 (2008). Available from www.nice.org.uk/TA145
- Improving outcomes in head and neck cancers: the manual. NICE cancer service guidance (2004). Available from www.nice.org.uk/csghn

Under development

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

- Intensity modulated radiotherapy for head and neck cancer. NICE technology appraisal guidance (suspended).

7 Proposed date for 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 It is proposed that the guidance on this technology is considered for review in June 2012. The Institute would particularly welcome comment on this proposed date.

David Barnett
Chair, Appraisal Committee
January 2009

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.

Professor Keith Abrams

Professor of Medical Statistics, University of Leicester

Professor David Barnett (Chair)

Professor of Clinical Pharmacology, University of Leicester

Dr Peter Barry

Consultant in Paediatric Intensive Care, Leicester Royal Infirmary

Professor John Cairns

Public Health and Policy, London School of Hygiene and Tropical Medicine

Dr Mark Chakravarty

External Relations Director – Pharmaceuticals & Personal Health, Oral Care Europe

Professor Jack Dowie

Health Economist, London School of Hygiene and Tropical Medicine

Ms Lynn Field

Nurse Director, Pan Birmingham Cancer Network

Dr Fergus Gleeson

Consultant Radiologist, Churchill Hospital, Oxford

Ms Sally Gooch

Independent Nursing and Healthcare Consultant

Mrs Eleanor Grey

Lay member

Professor Gary McVeigh

Professor of Cardiovascular Medicine, Queens University, Belfast

Dr Neil Milner

General Practitioner, Tramways Medical Centre, Sheffield

Dr John Pounsford

Consultant Physician, Frenchay Hospital, Bristol

Dr Lindsay Smith

General Practitioner, East Somerset Research Consortium

Mr Cliff Snelling

Lay member

Professor Ken Stein

Professor of Public Health, Peninsula Technology Assessment Group (PenTAG), University of Exeter

Professor Andrew Stevens

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

Dr Rod Taylor

Associate Professor in Health Services Research, Peninsula Medical School, Universities of Exeter and Plymouth

Dr Colin Watts

Consultant Neurosurgeon, Addenbrookes Hospital

Mr Tom Wilson

Director of Contracts and Information Management and Technology, Milton Keynes PCT

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.

Nicola Hay

Technical Lead

Janet Robertson

Technical Adviser

Jeremy Powell

Project Manager

Appendix B: Sources of evidence considered by the Committee

A The Evidence Review Group (ERG) report for this appraisal was prepared by Liverpool Reviews & Implementation Group, University of Liverpool:

- Greenhalgh J, Bagust A et al. Cetuximab for recurrent and/or metastatic squamous cell carcinoma of the head and neck (SCCHN), November, 2008

B 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). Organisations listed in I were also invited to make written submissions. Organisations listed in II and III had the opportunity to give their expert views. Organisations listed in I II and III also have the opportunity to appeal against the final appraisal determination.

I Manufacturer/sponsor:

- Merck Serono

II Professional/specialist and patient/carer groups:

- British Association of Head and Neck Oncology Nurses
- British Association of Otorhinolaryngologists – Head and Neck Surgeons
- CLIC Sargent
- Let's Face It
- Macmillan Cancer Support
- Mouth Cancer Foundation
- National Association of Laryngectomee Clubs
- Rarer Cancers Forum
- Royal College of Nursing
- Royal College of Pathologists
- Royal College of Physicians, Medical Oncology Joint Special Committee

- Royal College of Radiologists

III Other consultees

- Department of Health
- Leicester City PCT
- 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
- Medac UK
- MRC Clinical Trials Unit
- National Collaborating Centre for Cancer
- NHS Quality Improvement Scotland
- Pharmacia
- Roche Diagnostics
- Welsh Association of Head and Neck Oncologists

C The following individuals were selected from clinical specialist and patient advocate nominations from the non-manufacturer/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 are invited to comment on the ACD.

- Mr Jan Dekowski, nominated by the Mouth Cancer Foundation – patient expert
- Mrs Julie Hewett, Macmillan Head & Neck CNS, South Devon Healthcare Foundation Trust, nominated by the British Association of Head and Neck Oncology Nurses – clinical specialist
- Mrs Marilyn Jones, nominated by the National Association of Laryngectomee Clubs – patient expert
- Dr Chris Nutting, Consultant Clinical Oncologist, Royal Marsden and Royal Brompton Hospitals, nominated by the Royal College of Physicians – clinical specialist
- Mr Vinidh Paleri, Consultant Surgeon, Newcastle upon Tyne Hospitals NHS Trust, nominated by the British Association of

Otolaryngologists – Head and Neck Surgeons – clinical specialist