NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

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

Expert statement declaration form

Please sign and return by email to:
jeremy.powell@nice.org.uk

If email is not possible, please return by fax to Jeremy Powell, Project Manager
on 020 7061 9830

or by post to: NICE, MidCity Place, 71 High Holborn, London WC1V 6NA

I confirm that:

- I agree with the content of the statement submitted by **Mouth Cancer Foundation** and consequently I will not be submitting a personal statement.

Name: Mr Dekowski

Signed:

Date: OCTOBER 24TH 2008

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I confirm that:

- I agree with the content of the statement submitted by the British Association of Head and Neck Oncology Nurses and consequently I will not be submitting a personal statement.

Name: Mrs Hewett

Signed:

Date: 10/10/8

Patient/carer organisation statement template

Thank you for agreeing to give us your views on the technology and the way it should be used in the NHS.

Patients and patient advocates can provide a unique perspective on the technology, which is not typically available from the published literature.

To help you give your views, we have provided a template. The questions are there as prompts to guide you. You do not have to answer every question. Please do not exceed the 8-page limit.

About you

Your name:

Name of your organisation: THE NATIONAL ASSOCIATION OF LARYNGECTOMEE CLUBS

Are you (tick all that apply):

- a patient with the condition for which NICE is considering this technology?
- a carer of a patient with the condition for which NICE is considering this technology?
- an employee of a patient organisation that represents patients with the condition for which NICE is considering the technology? If so, give your position in the organisation where appropriate (e.g. policy officer, trustee, *member, etc)*
- ✓ other? (please specify) I HAD A LARYNGECTOMEE FOR SCCHN EIGHT YEARS AGO; ALSO LOBECTOMY FOR SCC (R) LUNG TEN YEARS AGO AND A NUMBER OF SKIN SCC FORTUNATELY NO RECURRENCE SO FAR. BUT IT IS AN ANXIETY

What do patients and/or carers consider to be the advantages and disadvantages of the technology for the condition?

1. **Advantages**

(a) Please list the specific aspect(s) of the condition that you expect the technology to help with. For each aspect you list please describe, if possible, what difference you expect the technology to make.

- PEOPLE UNABLE TO HAVE CHEMOTHERAPY STILL HAVE ACCESS TO CETUXIMAB WITH RADIOTHERAPY
- PEOPLE ALREADY HAVING CETUXIMAB SHOULD NOT BE PREVENTED FROM CONTINUING TO BE PRESCRIBED WHEN HELPING WITH THE CONDITION
- PEOPLE WITH A KARNOFSKY PERFORMANCE-STATUS SCORE OF 90% ARE ABLE TO HAVE CETUXIMAB HOPEFULLY TO IMPROVE THEIR QUALITY OF LIFE

(b) Please list any short-term and/or long-term benefits that patients expect to gain from using the technology. These might include the effect of the technology on:

- *the course and/or outcome of the condition*
- physical symptoms
- pain
- level of disability
- *mental health*
- quality of life (lifestyle, work, social functioning etc.)
- other quality of life issues not listed above
- other people (for example family, friends, employers)
- *other issues not listed above.*

- THE TECHNOLOGY MIGHT PROLONG THE PATIENT'S LIFE
- IT MIGHT IMPROVE ANY PHYSICAL SYMPTOMS IF IT IS DESTROYING CANCER CELLS
- IF IT SHRINKS THE TUMOUR IT MIGHT HELP WITH ANY PAIN
- IT MIGHT IMPROVE BREATHLESSNESS LEADING TO AN IMPROVEMENT IN DISABILITY
- KNOWING THAT YOU ARE TAKING SOMETHING THAT MIGHT KILL CANCER CELLS WOULD ALLEVIATE ANXIETY LEADING TO AN IMPROVEMENT IN MENTAL HEALTH
- IF THE TECHNOLOGY LEADS TO AN IMPROVEMENT IN HEALTH AND WELLBING PATIENT MAY BE ABLE TO RETURN TO WORK
- MIGHT PREVENT ADMISSIONS TO HOSPITAL
- FAMILY, FRIENDS AND EMPLOYERS MIGHT FEEL PATIENT HAS A QUALITY OF LIFE AND NOT LIABLE TO "DROP DEAD" AT ANY TIME
- HELP PATIENT TO RETURN TO "NORMAL ACTIVITY" FOR AS LONG AS POSSIBLE

What do patients and/or carers consider to be the advantages and disadvantages of the technology for the condition? (continued)

2. **Disadvantages**
Please list any problems with or concerns you have about the technology.
Disadvantages might include:
- aspects of the condition that the technology cannot help with or might make worse.
- difficulties in taking or using the technology
- side effects (please describe which side effects patients might be willing to accept or tolerate and which would be difficult to accept or tolerate)
- impact on others (for example family, friends, employers)
- financial impact on the patient and/or their family (for example cost of travel needed to access the technology, or the cost of paying a carer).

- THERE ARE INFUSION-RELATED REACTIONS AND IF PATIENTS ALREADY HAVE BREATHING DIFFICULTIES THIS CAN BE MADE WORSE.
- IF A PATIENT HAS POOR VEINS THIS CAN PRESENT DIFFICULTIES IN ADMINISTRATION
- A PATIENT MIGHT FIND IT DIFFICULT TO ADJUST TO A VERY BAD SKIN REACTION BUT WOULD BE ABLE TO PUT UP WITH REGULAR BLOOD TESTS TO MONITOR ELECTROLYTES
- FAMILY, FRIENDS, EMPLOYERS MIGHT BE WORRIED WHETHER TECHNOLOGY WILL IMPROVE OR MAKE THINGS WORSE FOR PATIENT
- THE PATIENT MAY HAVE TO TRAVEL A LONG DISTANCE TO ACCESS THE TECHNOLOGY EG NOT TO A LOCAL HOSPITAL, BUT A CENTRE OF EXCELLENCE WHICH MIGHT BE MILES AWAY

3. Are there differences in opinion between patients about the usefulness or otherwise of this technology? If so, please describe them.

I HAVE SPOKEN TO A NUMBER OF PATIENTS AND MEMBERS OF SUPPORT GROUPS AT NALC AND THEY WERE ALL IN AGREEMENT ABOUT THE USEFULNESS OF THIS TECHNOLOGY

4. Are there any groups of patients who might benefit **more** from the technology than others? Are there any groups of patients who might benefit **less** from the technology than others?

ALL GROUPS OF PATIENTS HAVE THEIR OWN CHOICES BUT I FIRMLY BELEIVE THE TECHNOLOGY SHOULD BE OPEN TO ALL PATIENTS

Comparing the technology with alternative available treatments or technologies

NICE is interested in your views on how the technology compares with with existing treatments for this condition in the UK.

(i) Please list any current standard practice (alternatives if any) used in the UK.

- PLATINUM - BASED CHEMOTHERAPY WITH RADIOTHERAPY

(ii) If you think that the new technology has any **advantages** for patients over other current standard practice, please describe them. Advantages might include:

- *improvement in the condition overall*
- improvement in certain aspects of the condition
- ease of use (for example tablets rather than injection)
- where the technology has to be used (for example at home rather than in *hospital*)
- side effects (please describe nature and number of problems, frequency, duration, severity etc.)

- TUMOUR MIGHT SHRINK
- CETUXIMAB MIGHT NOT HAVE ALL THE SIDE-EFFECTS OF PLATINUM BASED CHEMOTHERAPY
- CETUXIMAB IS GIVEN BY INJECTION WEEKLY SO AVOIDS DAILY TABLETS.
- SIDE-EFFECTS CAN INCLUDE NAUSEA, VOMITING, SKIN REACTIONS SHORTNESS OF BREATH - THE SAME AS OTHER "MEDICATIONS"

(iii) If you think that the new technology has any **disadvantages** for patients compared with current standard practice, please describe them. Disadvantages *might include:*

- worsening of the condition overall
- worsening of specific aspects of the condition
- difficulty in use (for example injection rather than tablets)
- where the technology has to be used (for example in hospital rather than at home)
- side effects (for example nature or number of problems, how often, for how long, how severe).

- THE DISADVANTAGES ARE THE SAME FOR ANY CHEMOTHERAPEUTIC TECHNOLOGY.
- THE CONDITION COULD WORSEN BECAUSE OF THE EXTREME SIDE EFFECTS OF THE TECHNOLOGY IE CARDIOPULMONARY
- HAVING TO HAVE DRUGS INTRAVENOUSLY BY INJECTION INSTEAD OF ORALLY.
- HAVING TO MAKE THE TREK TO HOSPITAL WEEKLY
- THE SIDE-EFFECTS COULD BE AS BAD OR WORSE EG. NAUSEA, VOMITING, SKIN REACTIONS ETC

Research evidence on patient or carer views of the technology

Availability of this technology to patients in the NHS

What key differences, if any, would it make to patients and/or carers if this technology was made available on the NHS?

IF THIS TECHNOLOGY WAS AVAILABE IN THE NHS THE DIFFERENCES IT WOULD MAKE INCLUDE

- PATIENTS WITH A METASTATIC SPREAD MIGHT FEEL THERE WAS SOME HOPE FOR A LONGER QUALITY OF LIFE
- CARERS, FAMILY AND FRIENDS MIGHT FEEL THAT IT WAS NOT "THE END"

What implications would it have for patients and/or carers if the technology was not made available to patients on the NHS?

- THAT ONCE THE PERSON KNEW THEY HAD A METASTATIC SPREAD IT WAS JUST A MATTER OF TIME BEFORE DEATH
- LOOKING TO GET THE DRUG AT ANY COST, USING UP HARD-EARNED MONEY AND CAUSING ANXIETY +++

Are there groups of patients that have difficulties using the technology?

- ELDERLY PEOPLE, WHO ARE DISABLED WITHOUT CARERS TO HELP
- PEOPLE WITH LEARNING DIFFICULTIES DEPENDENT ON CARERS

Other issues

Please include here any other issues you would like the Appraisal Committee to consider when appraising this technology.

END OF LIFE ISSUES CAUSE HUGE ANXIETIES FOR MANY PEOPLE AND IF THERE IS THE POSSIBILITY OF PATIENTS EXTENDING THEIR LIFE WITH THIS TECHNOLOGY THEY SHOULD BE GIVEN THE OPPORTUNITY. SOME PATIENTS OF COURSE WILL CHOOSE NOT TO DO SO.

If you are familiar with the evidence base for the technology, please comment on whether patients' experience of using the technology as part of their routine NHS care reflects that observed under clinical trial conditions.

I have READ AS MUCH AS I CAN ABOUT THE TECHNOLOGY FOR CETUXIMAB AND KNOW BASICALLY HOW IT WORKS BY BLOCKING THE HUMAN GROWTH FACTOR RECEPTOR (EGFR) AND INHIBITING THE PROLIFERATION OF CELLS. I HAVE NO KNOWLEDGE OF ANYBODY USING THIS TECHNOLOGY UNDER CLINICAL TRIAL CONDITIONS

Are there any adverse effects that were not apparent in the clinical trials but have come to light since, during routine NHS care?

AS MENTIONED ABOVE I HAVE NO KNOWLEDGE PERSONALLY OF CLINICAL TRIALS

Are you aware of any research carried out on patient or carer views of the condition *or existing treatments that is relevant to an appraisal of this technology? If yes,* please provide references to the relevant studies.

NO I DO NOT

Clinical expert statement template

Thank you for agreeing to give us a statement on your organisation's view of the technology and the way it should be used in the NHS.

Healthcare professionals can provide a unique perspective on the technology within the context of current clinical practice which is not typically available from the published literature.

To help you in making your statement, we have provided a template. The questions are there as prompts to guide you. It is not essential that you answer all of them.

Please do not exceed the 8-page limit.

About you

Your name: Dr Christopher Nutting

Name of your organisation: Royal Marsden NHS Trust

Are you (tick all that apply):

- a specialist in the treatment of people with the condition for which NICE is considering this technology? Yes
- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)? Yes
- an employee of a healthcare professional organisation that represents clinicians treating the condition for which NICE is considering the technology? If so, what is your position in the organisation where appropriate (e.g. policy officer, trustee, member etc.)? No
- other? (please specify)

What is the expected place of the technology in current practice?

Recurrent or metastatic head and neck cancer is a common clinical problem. The current treatment standard for fit patients is platinum based chemotherapy schedules. Cisplatin and 5fluorouracil combined represents the standard of care in the Western world. In patients with contraindications to cisplatin such as poor renal or cardiac function and in patients with neuropathy, carboplatin is often substituted.

The above treatment is given under specialist supervision of a clinical or medical oncologist based in a cancer treatment unit or center.

The technology being assessed is the addition of an anti-epidermal growth factor antibody, cituximab (Erbitux) to the standard chemotherapy described above.

A large multi-center randomised trial was performed in Europe including UK centers and was published in the New England Journal of Medicine (Vermorken et al NEJM 2008;359(11):1116-27).

The trial concluded that a statistically significant prolongation of life was observed in those patients who received chemotherapy plus cituximab, compared to the standard chemotherapy alone (10.1 months compared to 7.4 months p=0.04). The addition of cituximab to chemotherapy increased the response rate from 20% to 36% (p<0.001). cituximab administration was associated with an increased risk of sepsis, skin rash and infusion reactions (see abstract below).

This trial represents a well conducted investigation which for the first time shows a prolongation of life for patients with head and neck cancer. The absolute prolongation of life is modest, but the increased response rate rates to this new therapy are particularly important as head and neck tumours typically grow in the airway and upper GI tract, and interfere with basic functions of swallow, breathing and speech. No quality of life data on this trial has yet been presented to my knowledge.

Implementation of this new therapy to the NHS would be associated with increased cost of both the cituximab medication itself, and also increased administration costs.

It is my opinion that cituximab combined with cisplatin or carboplatin and 5 fluorouracil represents the standard of care for patients with recurrent or metastatic head and neck cancer and as such should be made available to NHS patients using the criteria of the above trial.
I fear that NICE may not approve it on cost effectiveness grounds.

Abstract

BACKGROUND: Cetuximab is effective in platinum-resistant recurrent or metastatic squamous-cell carcinoma of the head and neck. We investigated the efficacy of cetuximab plus platinum-based chemotherapy as first-line treatment in patients with recurrent or metastatic squamous-cell carcinoma of the head and neck. METHODS: We randomly assigned 220 of 442 eligible patients with untreated recurrent or metastatic squamous-cell carcinoma of the head and neck to receive cisplatin (at a dose of 100 mg per square meter of body-surface area on day 1) or carboplatin (at an area under the curve of 5 mg per milliliter per minute, as a 1-hour intravenous infusion on day 1) plus fluorouracil (at a dose of 1000 mg per square meter per day for 4 days) every 3 weeks for a maximum of 6 cycles and 222 patients to receive the same chemotherapy plus cetuximab (at a dose of 400 mg per square meter initially, as a 2-hour intravenous infusion, then 250 mg per square meter, as a 1-hour intravenous infusion per week) for a maximum of 6 cycles. Patients with stable disease who received chemotherapy plus cetuximab continued to receive cetuximab until disease progression or unacceptable toxic effects, whichever occurred first. RESULTS: Adding cetuximab to platinum-based chemotherapy with fluorouracil (platinum-fluorouracil) significantly prolonged the median overall survival from 7.4 months in the chemotherapy-alone group to 10.1 months in the group that received chemotherapy plus cetuximab (hazard ratio for death, 0.80; 95% confidence interval, 0.64 to 0.99; P=0.04). The addition of cetuximab prolonged the median progression-free survival time from 3.3 to 5.6 months (hazard ratio for progression, 0.54; P<0.001) and increased the response rate from 20% to 36% (P<0.001). The most common grade 3 or 4 adverse events in the chemotherapy-alone and cetuximab groups were anemia (19% and 13%, respectively), neutropenia (23% and 22%), and thrombocytopenia (11% in both groups). Sepsis occurred in 9 patients in the cetuximab group and in 1 patient in the chemotherapy-alone group (P=0.02). Of 219 patients receiving cetuximab, 9% had grade 3 skin reactions and 3% had grade 3 or 4 infusion-related reactions. There were no cetuximab-related deaths. CONCLUSIONS: As compared with platinum-based chemotherapy plus fluorouracil alone, cetuximab plus platinum-fluorouracil chemotherapy improved overall survival when given as first-line treatment in patients with recurrent or metastatic squamous-cell carcinoma of the head and neck.

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I confirm that:

- I agree with the content of the statement submitted by the British Association of Otolaryngologists-Head and Neck Surgeons and consequently I will not be submitting a personal statement.

Name: Mr Vinidh

Signed:

Date: 11/2/08