NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Cetuximab for LASCCHN

Response to consultee, commentator and public comments on the ACD

Consultee	Comment	Institute response
Merck Serono	Merck Serono appreciates the opportunity to comment on the evidence base used to inform NICE's preliminary decision regarding cetuximab for the treatmenbt of locally advanced squamous cell carcinoma of the head and neck (LA SCCHN). We would like to comment on/request clarification with regards to two items under point 1 of the general headings requested	See below for response to detailed comments.
	i) Do you consider that all the relevant evidence has been taken into account? 1. <u>Request for clarity as to the evidence to justify the inclusion of carboplatin as comparative treatment for patients with LA SCCHN</u> In section 4.9 of the ACD, the Appraisal Committee considers the use of platinum based chemoradiotherapy and discusses the use for this group of patients: "*The Committee was aware 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 regimens have been studied in this condition and are used to treat this condition in UK clinical practice*" It is clear from clinical opinion attained from commentators to this appraisal that carboplatin can be used, albeit rarely for patients who are contraindicated for cisplatin based treatments. Carboplatin may be considered to be "used", but not, "routinely".	Comment noted. FAD section 4.9 amended to *'…carboplatin-based regimens have been studied in this condition and are sometimes used to treat this condition in UK clinical practice.'*

Consultee	Comment	Institute response
Merck Serono (continued)	The literature review submitted as part of Merck Serono's response to questions provided on the 15th October 2007, identified that carboplatin had also been, "studied". However this literature review failed to identify any robust evidence to support the use of carboplatin in the treatment of LA SCCHN. The most robust source identified was from Jeremic et al where the 53 patients treated with carboplatin in combination with radiotherapy reported a median overall survival benefit of 30 months. Indeed clinical opinion from commentators to this appraisal also failed to identify a robust source to prove the efficacy of carboplatin based chemoradiotherapy.	Comment noted
	Greater clarity would be appreciated as to the source of information utilized by the Appraisal Committee to include carboplatin as a comparator. This clarity will guide future appraisals in this area as to the accepted efficacy and tolerability of carboplatin and increase clarity of NICE guidance to patients who will question why it is appropriate to be prescribed an unproven, yet studied, medication rather than a proven, licensed alternative such as cetuximab.	Comment noted. See FAD section 3.13 and 4.9. The Appraisal Committee does not make recommendations about comparator treatments, that is, alternative treatments with which the treatment under appraisal is compared. Carboplatin-based chemoradiotherapy is considered as a comparator in this appraisal. Consideration of comparator treatments 'off licence' is appropriate when such treatment is considered part of current practice in the NHS (see section 2.2.3.1 of the Guide to the Methods of Technology Appraisal).

Consultee	Comment	Institute response
Merck Serono (continued)	2. <u>Update of information on available cetuximab vial sizes presented in section 2.3</u> Section 2.3 of the ACD presents information on the acquisition cost and available vial sizes of cetuximab from the BNF edition 54. since this publication Merck Serono has launched an alternative formulation of cetuximab and information is presented below as in the January 2008 edition of Mims: *Cetuximab* *50mg/ml soln in vial,* *20ml = £136.50:100ml = £682.50* The 2mg/ml formulation is no longer marketed. It would be greatly appreciated if this information could be updated.	Comment noted. Amendment made. See FAD section 2.3
Nominated Clinical Expert- Nick Slevin	Thank you for the opportunity to comment on the Appraisal consultation document and evaluation report on Cetuximab with radiotherapy in locally advanced head and neck cancer. From my reading of all the evidence submitted, I believe the summary of considerations in the ACD (para 4.11) perfectly describes the current indication for Cetuximab in our clinical practice.	Comment noted.
British Association of Head and Neck Oncologists	Thank you for asking BAHNO to reply to the single technology appraisal on Cetuximab. I have been nominated to do so on their behalf. I note that the ERG have reviewed the academic data which mostly consists of the Bonner study and have extracted a subgroup analysis supporting the use of Cetuximab plus radiotherapy in patients with KP greater than 90 but not in the poorer performance group. The company submission had however been for use in that poorer group of patients. Also the ERG states clearly that the current gold standard is chemoradiotherapy and Cetuximab should therefore be used in patients unable to have either Carboplatin or Cisplatin but for medical reasons unlikely to compromise their performance status.	Comment noted

Consultee	Comment	Institute response
British Association of Head and Neck Oncologists (continued)	I am unaware of any other mature data and feel that the ERG reliance on one source i.e. the Bonner trial is appropriate. The reasoning behind the decisions and the cost benefit analysis seem clear and whilst not unambiguous the pros and cons appear to have been worked through thoroughly and transparently.	Comment noted
	The UK oncology community acknowledges that there is diversity in practice nationally. There is a natural desire to employ an effective drug without increasing the radiotherapy toxicity and this appears to be a reasonable compromise. Many reasonably fit patients are older and the risks of chemoradiotherapy may outweigh the benefits. The possibility of an active combination treatment is attractive and overall I welcome the group's reasonable decision.	Comment noted
The National Association of Larygectomee Clubs	NALC has been grateful for the opportunity to take a formal part in the decision processes undertaken, by NICE, on the use of “Cetuximab for the treatment of locally advanced squamous cell cancer of the Head and Neck” and hope that our inclusion will help NICE to understand the priorities of patients and carers. As an organisation led and managed by patients and supported by carers we do have difficulties with some of the technical and medical evidence. Our remarks are based on our ‘user’ perception of the debate. NALCs concern is that our stance is not seen as that of ” patients wanting the latest drug”. It is about how the development of better and less toxic treatments may be progressed as quickly as possible to reduce the need for more serious and traumatic interventions. It will furthermore give the patient a choice of treatment not available at present.	Comment noted. Comments noted. The Appraisal Committee acknowledged the high risk of adverse effects of chemoradiotherapy and that cetuximab was a useful option because of its relatively low toxicity profile compared with chemotherapy. See FAD section 4.3.

Consultee	Comment	Institute response
The National Association of Larygectomee Clubs (continued)	ACD Feb. 2008 i) We consider that because of the rarity of these conditions the evidence needs to be viewed in a more flexible manner, especially in relation to the NHS economic argument, and the problems concerning the numbers of suitable patients for the research purposes. We are concerned that the relatively small numbers in the cohorts in each of the categories under consideration for the use of cetuximab are to continue to restrict appropriate consideration of the merits of these treatments. In addition we feel that the facts illustrating that the mortality rate has not changed ad new drug has been identified in four or more decades should have been given some weighting. We further consider that the question of the toxicity of platinum based chemotherapy, particularly its sue as an adjunct to radiotherapy, has also not been given sufficient thought.	Comment noted. The Appraisal Committee takes into account a number of factors during its decision making. See section 6 'Guide to the methods of Technology Appraisals' available at URL http://www.nice.org.uk/niceMedia/pdf/TAP_Methods.pdf Comments noted. The Appraisal Committee acknowledged the high risk of adverse effects of chemoradiotherapy and that cetuximab was a useful option because of its relatively low toxicity profile compared with chemotherapy. See FAD section 4.3.
	ii) We consider that the evidence of the rarity of head and neck cancers have not been given any weighting in the appraisal from the beginning of this whole process especially in relation to the economic , cost effectiveness question. Other financial considerations also have not been addressed such as, that given the rarity, numbers to be treated will be relatively low, as will the consequential costs to the health sector.	The Committee does not consider budget impact in its deliberations.
	It would also appear that when considering NHS costs the review failed to take into account the long term and ongoing costs to Primary and Social Care of supporting patients who undergo conservative surgery for these conditions.	The perspective taken for the evaluation of costs and outcomes in NICE Technology Appraisals is that of the NHS and Personal Social Services (PSS). This position reflects the remit from the Department Health to NICE

Consultee	Comment	Institute response
The National Association of Larygectomee Clubs (continued)	While we welcome the suggestions on research: (ACD:Page 16:32) NALC has members working as consumers in the research field and we are aware that proposals for research using cetuximab answering just the questions you require are being hampered by the lack of NICE recognition of the drug. We suggest that the last 3 paragraphs (page 7: the evaluation Report) are considered very seriously even if it is just that you provide a "within research" recommendation. This should speed up research proposals considerably.	Comment noted.
	A number of our comments and opinions in this review were put forward at the initial hearing and when the expert patients were required to leave the hearing our representative understood that these views were to be fully taken into account. However, when attempting to understand the final appraisal finds we found it difficult to trace and particular mention of those discussions wither in the first appraisal or the following appeal attended by both our representative as observers. For this reason we hope that our comments do not seem at odds with the documentation or out of kilter with the rest of the evidence. Again, thank you for our inclusion in this process.	Comment noted. The Committee heard from the clinical specialists and patient experts 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. See FAD section 4.3.

Consultee	Comment	Institute response
The Royal College of Pathologists	NICE Single Technology Appraisal (STA) - Cetuximab for the treatment of head and neck cancer Comments on Appraisal Consultation Document (ACD) As far as can be judged from the information provided in the Evaluation Report and a recent Mini Review on the subject (Reuter et al British Journal of Cancer 2007;96:408-416) all of the relevant evidence appears to have been taken into account by the Appraisal Committee to provide its provisional recommendations for the preparation of the guidance to the NHS. The ACD points out that the success of cetuximab plus radiotherapy over radiotherapy alone recorded by a single randomised clinical trail (RCT) is not appropriate to recommend extrapolation of its use for patients otherwise eligible for chemoradiotherapy, which is the current standard care. To cover this weakness the Committee has recommended conduction of "head-to-head trials of cetuximab in combination with radiotherapy versus chemoradiotherapy" to allow a more objective assessment of the benefit of cetuximab plus radiotherapy as a novel therapy for head and neck cancer. This message is echoed by the Minireview.	Comment noted.
Welsh Association of Head and Neck Oncologists	This is the response of the Welsh Association of Head and Neck Oncologists to the preliminary appraisal of Cetuximab for the treatment of locally advanced squamous cell cancer of the head and neck. WAHNO supports the appraisal committee's preliminary recommendations for the use of Cetuximab in combination with radiotherapy for patients with locally advanced squamous cell cancer of the head and neck as stated in sections 1.1 and 1.2 of the appraisal consultation document.	Comment noted.
Let's Face It	On reading through your report, I feel that Merck Serona need to do further research to prove their case.	Comment noted.
	I do consider that all the relevant evidence has been taken into account.	Comment noted.

Consultee	Comment	Institute response
Let's Face It (continued)	The summaries of clinical and cost effectiveness leaves my head swimming and as a patient cost is irrelevant if the drug is successful.	Comment noted. NICE publishes three versions of technology appraisal guidance. The full guidance of the appraisal (the recommendation and a summary of all the evidence), a quick reference guide (a short version for healthcare professionals) and Understanding NICE Guidance (a description of the guidance written for people with a specific condition).
	I consider that the provisional recommendations of the Appraisal Committee are sound and provide a suitable base for the preparation of guidance to the NHS.	Comment noted.
	I feel the need for special consideration be given to the use of Cetuximab for the patients who are slowly dying of head and neck cancer. These patients die long and lingering deaths as the tumours fill their mouths obstructing airways / eating and speaking. If the drug combined with radiotherapy can shrink these tumours then this will provide a more dignified route to death. helping not only the patient but their families and loved ones also the professionals who care for them.	Comment noted.
Royal College of Nursing	**Introduction** With a membership of over 400,000 registered nurses, midwives, health visitors, nursing students, health care assistants and nurse cadets, the Royal College of Nursing (RCN) is the voice of nursing across the UK and the largest professional union of nursing staff in the world. RCN members work in a variety of hospital and community settings in the NHS and the independent sector. The RCN promotes patient and nursing interests on a wide range of issues by working closely with the Government, the UK parliaments and other national and European political institutions, trade unions, professional bodies and voluntary organisations. The Royal College of Nursing welcomes the opportunity to review the Appraisal Consultation Document of the health technology appraisal of the use of Cetuximab for the treatment of head and neck cancer.	

Consultee	Comment	Institute response
Royal College of Nursing (continued)	**Response to the Appraisal Consultation Document** The Appraisal Consultation Document is comprehensive. The RCN welcomes the recommendation on the use of Cetuximab in combination with radiotherapy as a treatment option for patients with locally advanced squamous cell cancer of the head and neck.	Comment noted

Reply received but no comments:
Department of Health

Comments received from website consultation:
None