National Institute for Health and Clinical Excellence

Proposed Health Technology Appraisal

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

Consultees and commentators responses on the draft scope [pre-referral]

Comment 1: the draft remit

Section	Consultees	Comments	Response
Appropriateness	Lets face it	Most definitely	Comment noted
	Merck Serono	Merck Serono considers that this is a highly appropriate and urgent topic. Patients with recurrent or metastatic SCCHN have limited active treatment options. There is an important clinical need for further active lines of treatment for this poorly served group of patients.	Comment noted
	Mouth Cancer Foundation	Yes	Comment noted
	Rarer Cancers Forum	Very appropriate indeed there is little enough for these patients	Comment noted
Wording	Lets face it	The wording is explicit and precise	Comment noted
	Merck Serono	Merck Serono considers that the remit is appropriate.	Comment noted
	Mouth Cancer Foundation	Yes	Comment noted
	Rarer Cancers Forum	We wonder if for this number of patients a year it would be worth giving this drug orphan status and take that into account when considering the QALY.	Granting orphan status is outside the Institute's remit. The Institute does not have separate methods and processes for appraising rare diseases.

Section	Consultees	Comments	Response
Timing Issues	Merck Serono	Merck Serono would suggest that this topic is urgent. Patients with recurrent or metastatic SCCHN have limited active treatment options. There is an important clinical need for further active lines of treatment for this poorly served group of patients.	Comment noted
	Mouth Cancer Foundation	Yes	Comment noted
	Rarer Cancers Forum	We feel that any treatment to help this group of patients is urgent but would like to know if undertaking a draft scope prior to the licence will hasten the process	Please see the 'Guide to the single technology appraisal process' section 1.1.2 and 3.1.1.6.

Comment 2: the draft scope

Section	Consultees	Comments	Response
Background information	Lets face it	The information on head & neck cancers is accurate.	Comment noted
	Merck Serono	We would propose one amendment to this information: The last paragraph last sentence concerning SIGN guidelines would be clearer as follows: "Recent SIGN guidelines (2006) on the diagnosis and management of head and neck cancer recommend that patients with adequate performance status should be considered for platinum based chemotherapy as palliative chemotherapy in patients with recurrent and or metastatic head and neck cancer."	Scope amended
	Mouth Cancer Foundation	Yes	Comment noted
	Rarer Cancers Forum	Yes	Comment noted
The technology/ intervention	NCRI Clinical Studies Groups/RCP/ RCR/JCCO/ ACP	The Phase III trial is called EXTREME, and has completed. The data from the trial have been presented at recent international meetings and show a survival advantage for cetuximab + cisplatin +5FU over the standard of cisplatin + 5FU alone.	Scope amended to reflect the update on the clinical study.
	Let face it	As a patient I hesitate to approve the technology.	Comment noted

Section	Consultees	Comments	Response
The technology/ intervention (continued)	Merck Serono	We would propose this amendment to the second paragraph: Cetuximab does not yet have a UK marketing authorisation for the treatment of metastatic and/or recurrent SCCHN. However, EXTREME, the randomised phase III clinical trial examining the effect of first-line combination of Cetuximab plus cisplatin or carboplatin and 5-fluorouracil compared to cisplatin or carboplatin and 5-fluorouracil only has now completed. The Primary endpoint results were presented at ASCO 2007. The full data set was presented at ECCO 2007. The opinion of Merck Serono is that the intervention should be described as: "Cetuximab plus platinum based therapy"	Scope amended
	Mouth Cancer Foundation	Yes	Comment noted
	Rarer Cancers Forum	Yes	Comment noted
Population	Lets face it	No, I believe all groups are well covered.	Comment noted
	Merck Serono	The population is appropriately defined.	Comment noted
	Mouth Cancer Foundation	Should it not be available for all head and neck cancer patients if it avoids the sides effects of current treatments?	Technologies are appraised in accordance with their licensed indications. The Institute has already published guidance on the use of cetuximab for the treatment of locally advanced squamous cell carcinoma of the head and neck (SCCHN) in combination with radiation therapy (TA145).
Population (continued)	Rarer Cancers Forum	Yes	Comment noted

Section	Consultees	Comments	Response
Comparators	Lets face it	I believe Cetuximab to be a better alternative care than is now available to h/n patients. It provides a better quality of life, raising the patient's self esteem whilst experiencing the most traumatic side effects of chemo/radiotherapy.	Comment noted
	Merck Serono	This would seem to represent the current standard of care.	Comment noted
	Mouth Cancer Foundation	Yes	Comment noted
	Rarer Cancers Forum	Yes	Comment noted
Outcomes	Lets face it	The most important outcome of the technology will benefit the patient immeasurably. Shrinking the tumour, overall survival and quality of life. Far less adverse effects of treatment.	Comment noted
	Merck Serono	We are satisfied that these outcome measures are adequate	Comment noted
	Mouth Cancer Foundation	Yes	Comment noted
	Rarer Cancers Forum	Yes	Comment noted
Economic analysis	Lets face it	Cost effectiveness of treatment should take into account the fewer hospital beds required for patients.	Comment noted
	Merck Serono	The economic analysis is appropriate. The appropriate time horizon for assessment must take into account the average age of the intended patient population; however it would be reasonable to suggest that costs and benefits can be achieved within 5 – 10 years of treatment initiation.	Following the scoping workshop the scope has been amended to include a lifetime time horizon.

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	Rarer Cancers Forum	Have done above re the problem with the maketing authorisation	Comment noted
Other considerations	Lets face it	The patients who will benefit are the the Palliative care patients. Their need to die with dignity is an additional issue.	Comment noted
	Merck Serono	Merck Serono are not aware of any subgroups of patients that can be identified at this time.	Comment noted
Questions for consultation	NCRI Clinical Studies Groups/RCP/ RCR/JCCO/ ACP	The questions for consultation are incorrect: 1. The context is not first line. Most of these patients will have had surgery, radiotherapy and/or chemotherapy before. 2. There is no strong data to suggest that cetuximab should be used in patients unsuitable for chemotherapy. This question is inappropriate.	1) Following the discussion at the scoping workshop it was concluded that the remit would not be revised to include 'first line use'. 2) Comment noted.
	Merck Serono	1. The title of the appraisal should refer to first line use. 2. In recurrent and metastatic disease the standard of care would be chemotherapy using platinum based regimes. 3. Routinely patients with a KPS of 80 – 100 (WHO 0 -1) would be considered suitable for palliative chemotherapy in this setting. There is considerable clinical variation with regard to co-morbidities in this group of patients. There are some patients who may currently be considered for treatment with a KPS of 70 (WHO 2). 4. The trial data would not support first line use as a mono therapy in patients who are unsuitable for chemotherapy. There is data for patients who have progressed on platinum based therapy.	1) Following the discussion at the scoping workshop it was concluded that the remit would not be revised to include 'first line use'. 2) Following discussion at the scoping workshop the scope has been amended. 3) Comment noted. 4) Comment noted.
	Mouth Cancer Foundation	The consultation should examine cetuximab as a first-line treatment too.	Following the discussion at the scoping workshop it was concluded that the remit would not be revised to include 'first line use'.

Section	Consultees	Comments	Response
Questions for consultation (continued)	British Association of Head and Neck Oncologists (BAHNO)	**The manufacturer's pivotal phase three trial examines cetuximab as a first-line treatment. Should the title of the appraisal specifically refer to first-line use?** It is my opinion and as a oncologic surgeon, because of cost the use of cetuximab should be confined to usage within a randomised controlled trial only. It is important to separate from its usage in metastatic disease – one assumes patients within one of two clinical groups 1) neck metastases only and these would be operable and inoperable and 2) patients who have evidence of distant metastases – usually chest metastases. Currently with the increased usage of chemoradiotherapy, platinum products and radiotherapy the boundary between these patients is blurred ! I would suggest a trial for patients who have inoperable metastatic neck disease whose primary squamous cell carcinoma is located to the larynx, and oro – hypopharynx be enrolled – then we would be able to demonstrate its effectiveness. Of course the use of radiotherapy would need to defined and given appropriately!	Comment noted.
		What is considered to be the standard care for people with SCCHN? How is best supportive care/palliative care defined in this patient group? In summary the best standard of care is complete eradication of the tumour, with preservation of life and function! Some tumours can be best treated by surgery alone, some by radiotherapy alone, and others with stage III or IV disease may be suitable for chemoradiotherapy with surgical salvage on offer when the tumour fails to respond. However many of our patients are inoperable, and incurable at first presentation and hence require symptom treatment, and prolongation of independent survival with reasonable preservation of quality of life! Best supportive / palliative care is by my definitions: adequate information given to patient and their carers about what can be expected from current treatments available, the need for symptom control or preservation of functions – pain, breathing, swallowing, voice, speech, cosmesis – as well as physical, psychological and religious support being available when required or requested, and the ability to die, when indicated or when inevitable with a lucid mind, a peaceful psyche, and family support, preferably in ones own bed and home environment.	Comment noted

Section	Consultees	Comments	Response
Questions for consultation (continued)	BAHNO (continued)	**What is considered an adequate performance status for people receiving chemotherapy for metastatic and/or recurrent SCCHN?** Because patients with recurrent or metastatic disease are generally incurable, the goal of treatment are more limited, and include prolongation of overall survival or progression-free survival, palliation of existing symptoms, and prevention of new cancer-related symptoms. There has been no convincing evidence of patient benefit such as symptom reduction or improvement in quality of life and tumour shrinkage. The benefits to be derived are patient driven and require clinical trials to evaluate their symptoms and quality of life benefits. Generally a Karnovsky Score of 50 or more – but can be patient dependant – poor performance status, the presence of comorbidity, poor cognitive functioning, lack of social support, and ongoing use of tobacco and alcohol usage --- "The typical Head and Neck Cancer Patient".	Comment noted.
		Would cetuximab be used in patients considered unsuitable for chemotherapy? The current used chemotherapy in head and neck cancer is a platinum based drugs – cis - or carbo -platin with 5 F-U. The platinum drugs are nephrotoxic, and thus are contraindicated when renal function is dysfunctional. Thus when patient have been considered unsuitable for radiation and cisplatin, then the use of cetuximab and radiotherapy may be indicated in patients who are over 70 years of age, who have active peripheral, cerebral, coronary vascular disease, patients who have impaired renal function, patients who have tried cisplatin in the neoadjuvant setting and have been found to be intolerant and of course patients choice when informed of its potential benefits against current conventional alternative treatments.	Comment noted.
Additional comments on the draft scope.	NCRI Clinical Studies Groups/RCP/ RCR/JCCO/ ACP	Other than the factual inaccuracies above the draft scope is OK.	Comment noted

Comment 4: Regulatory issues

Section	Consultees	Comments	Response
Remit	Merck Serono	Commercial in Confidence information removed	Comment noted
Current or proposed marketing authorisation	Merck Serono	***What are the current indications for the technology?*** o Treatment of Epidermal Growth Factor Receptor-expressing metastatic colorectal cancer (mCRC) in combination with irinotecan after failure of irinotecan-including cytotoxic therapy. o Treatment of locally advanced squamous cell carcinoma of the head and neck (SCCHN) in combination with radiation therapy.	Comments noted
		What are the planned indications for the technology? Commercial in Confidence information removed	Comments noted
		What is the target date (mm/yyyy) for regulatory submission? Commercial in Confidence information removed	Comments noted
		Which regulatory process are you following? Centralised	Comment noted
		What is the anticipated date (mm/yyyy) of CHMP positive opinion (if applicable) and regulatory approval? Commercial in Confidence information removed	Comment noted
		Please indicate whether the information you provide concerning the proposed marketing authorisation is in the public domain and if not when it can be released. All commercial in confidence information must be highlighted and underlined. All information provided deemed as Commercial in Confidence is highlighted as such	Comment noted