NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of TA145; Cetuximab for the treatment of head and neck cancer

This guidance was issued in June 2009

The review date for this guidance is March 2011

Original remit(s)

To appraise the clinical and cost effectiveness of cetuximab in its licensed indications for refractory head and neck cancer.

Current guidance

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.

Recommendation

We recommend that NICE reconsider whether a review is necessary after June 2015 after the results of NCT00956007 become available. Until that time, the guidance should be transferred to the static list.

Rationale

One on-going trial of radiation therapy with or without cetuximab in treating patients who have undergone surgery for locally advanced head and neck cancer (NCT00956007) is expected to complete in June 2015. Its primary outcome is overall survival and has an estimated enrolment of 700 adults. It is therefore recommended that the decision to review this guidance be deferred until after 2015 when the results of NCT00956007 become available, when the degree to which the results of the trial impact on the recommendations in the current guidance are known. No other ongoing trials have an impact on this patient population or the current guidance.

New evidence

The search strategy from the original assessment report was re-run on the Cochrane Library, Medline, Medline In-Process and Embase. References from August, 2006 onwards were reviewed. Additional searches of clinical trials registries and other sources were also carried out. The results of the literature search are discussed in the 'Summary of evidence and implications for review' section below. See Appendix 2 for further details of ongoing and unpublished studies.

Summary of evidence and implications for review

At the time of the original appraisal, cetuximab was indicated, in combination with radiotherapy, for the treatment of patients with locally advanced squamous cell cancer of the head and neck. Since the publication of TA145, the indication has expanded to include use in combination with platinum-based chemotherapy, for recurrent and/or metastatic squamous cell cancer of the head and neck. This indication was appraised in TA 172, in which cetuximab in combination with platinum-based chemotherapy was not recommended for the treatment of metastatic and/or recurrent squamous cell carcinoma of the head and neck. Given the separate populations (locally advanced versus metastatic) and the separate combination therapies (radiotherapy versus platinum-based chemotherapy) covered in the respective components of the current indication, there appears no reason to combine the review of TA145 with that of TA172 (which is scheduled to be considered for review in June 2012).

Searching has identified two ongoing randomised controlled trials involving cetuximab in the relevant population. One trial compares the rate of radio-dermatitis in people receiving cetuximab in combination with radiotherapy with and without the local application of OTD70DERM. As both trial arms contain cetuximab, the results of this trial are not likely to impact on the recommendations in the current guidance. Another on-going trial of radiation therapy with or without cetuximab in treating patients who have undergone surgery for locally advanced head and neck cancer (NCT00956007) is expected to complete in June 2015. Its primary outcome is overall survival and has an estimated enrolment of 700 adults. It is therefore recommended that the decision to review this guidance be deferred until after 2015 when the results of NCT00956007 become available, as the degree to which the results of the trial may impact on the

recommendations in the original guidance is unclear at this time.

Implementation

No submission was received from Implementation.

Equality issues

The current guidance defines the population for whom cetuximab is recommended by Karnofsky performance-status score. Recommendation 1.3 therefore stipulates that "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."

No other equality issues were raised in the original guidance.

GE paper sign off: Frances Sutcliffe, 24 March 2011

Contributors to this paper:

Information Specialist:	Daniel Tuvey
Technical Lead:	Whitney Miller
Technical Adviser:	Eleanor Donegan
Project Manager:	Kate Moore
CPP/CPHE input	N/A

Appendix 1 – explanation of options

When considering whether to review one of its Technology Appraisals NICE must select one of the options in the table below:

Options	**Consequence**	**Selected – 'Yes/No'**
A partial review of the guidance should be planned into the appraisal work programme.	A partial review of the appraisal will be planned into the NICE's work programme.	No
The decision to review the guidance should be deferred to 2015.	NICE will reconsider whether a review is necessary after June 2015 after the results of NCT00956007 become available.	No
A review of the guidance should be combined with a review of a related technology appraisal.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the specified related technology.	No
A review of the guidance should be combined with a new technology appraisal that has recently been referred to NICE.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the newly referred technology.	No
The guidance should be incorporated into an on-going clinical guideline.	The on-going guideline will include the recommendations of the technology appraisal. The technology appraisal will remain extant alongside the guideline. Normally it will also be recommended that the technology appraisal guidance is moved to the static list until such time as the clinical guideline is considered for review. This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal.	No

Options	Consequence	Selected – 'Yes/No'
The guidance should be updated in an on-going clinical guideline.	Responsibility for the updating the technology appraisal passes to the NICE Clinical Guidelines programme. Once the guideline is published the technology appraisal will be withdrawn. Note that this option does not preserve the funding direction associated with a positive recommendation in a NICE Technology Appraisal. However, if the recommendations are unchanged from the technology appraisal, the technology appraisal can be left in place (effectively the same as incorporation).	No
The guidance should be transferred to the 'static guidance list'.	**The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider. Literature searches are carried out every 3 years to check whether any of the Appraisals on the static list should be flagged for review.** **NICE will reconsider whether a review is necessary after June 2015 after the results of NCT00956007 become available. Until that time, the guidance should be transferred to the static list.**	**Yes**

NICE would typically consider updating a technology appraisal in an ongoing guideline if the following criteria were met:

i. The technology falls within the scope of a clinical guideline (or public health guidance)

ii. The technology falls within the scope of a clinical guideline (or public health guidance)

iii. There is no proposed change to an existing Patient Access Scheme or Flexible Pricing arrangement for the technology, or no new proposal(s) for such a scheme or arrangement

iv. There is no new evidence that is likely to lead to a significant change in the clinical and cost effectiveness of a treatment

v. The treatment is well established and embedded in the NHS. Evidence that a treatment is not well established or embedded may include;

- Spending on a treatment for the indication which was the subject of the appraisal continues to rise
- There is evidence of unjustified variation across the country in access to a treatment
- There is plausible and verifiable information to suggest that the availability of the treatment is likely to suffer if the funding direction were removed
- The treatment is excluded from the Payment by Results tariff

vi. Stakeholder opinion, expressed in response to review consultation, is broadly supportive of the proposal.

Appendix 2 – supporting information

Relevant Institute work

Published

Cancer service guidance CSGHN. Service guidance on improving outcomes in head and neck cancers. Review date: unknown

Technology appraisals TA172 Cetuximab for the treatment of metastatic and/or recurrent squamous cell carcinoma of the head and neck. Published: June 2008; Review date: June 2012

Suspended/terminated

Technology appraisal. Contusugene ladenovec within its licensed indication for the treatment of unresectable recurrent and/or refractory squamous cell carcinoma of the head and neck. The manufacturer withdrew its application for a marketing authorisation.

Technology appraisal. Intensity modulated radiotherapy for head and neck cancer. The suspension was to allow NICE to consider the issues that emerged during the Consultee Information Meeting and to liaise with the Department of Health about how to best proceed with these appraisals.

In topic selection

Lapatinib for resectable and unresectable head and neck cancer (ID3022) NHSC considering

Lapatinib (Tyverb) for head and neck cancer ID5424) A-listed. NICE has requested briefing note from NHSC

Nimotuzumab (BIOMAb-EGFR) for head and neck cancer (ID5200) A-listed. NICE has requested briefing note from NHSC

Panitumumab for head and neck cancer (ID3033). Considered at Pre-scoping. It was agreed that this topic should continue through the appraisal process

Details of changes to the indications of the technology

Indication considered in original appraisal	Proposed indication (for this appraisal)
Cetuximab, in combination with radiotherapy, is licensed for the treatment of patients with locally advanced squamous cell cancer of the head and neck.	Cetuximab is indicated for the treatment of patients with squamous cell cancer of the head and neck • in combination with radiation therapy for locally advanced disease, • in combination with platinum-based chemotherapy for recurrent and/or metastatic disease.

Registered and unpublished trials

Trial name and registration number	Details
Radiation Therapy With or Without Cetuximab in Treating Patients Who Have Undergone Surgery for Locally Advanced Head and Neck Cancer (NCT00956007)	This randomized phase III trial is studying radiation therapy to see how well it works compared with radiation therapy given together with cetuximab in treating patients who have undergone surgery for locally advanced head and neck cancer. Number of participants: 700. Estimated Primary Completion Date: June 2015
Cetuximab With Radiotherapy for Locally Advanced Squamous Cell Carcinoma of the Head and Neck in Chinese Subjects (CHANCE) (NCT01012258)	To assess the antitumor activity and safety profile of cetuximab when given in combination with radiotherapy (RT) for the treatment of locally advanced squamous cell carcinoma of the head and neck (SCCHN) in Chinese subjects. Number of participants: 66. Estimated Study Completion Date: February 2014
Trial of OTD70DERM® in Radio-dermatitis Induced by Radiotherapy-Erbitux® (GORTEC 2009-01) (NCT01228565)	The aim of this randomized trial is to compare the rate of radio-dermatitis grade 2+ (NCI-CTC V3.0) in patients receiving radiotherapy+Erbitux+placebo versus in patients receiving radiotherapy+Ervitux+OTD70DERM® for the treatment of head and neck carcinoma. Number of participants: 70. Estimated Study Completion Date: February 2012