NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of TA172; Cetuximab for the treatment of metastatic and/or recurrent squamous cell carcinoma of the head and neck

This guidance was issued in June 2009.

The review date for this guidance is June 2012.

1. Recommendation

The guidance should be transferred to the 'static guidance list'.

That we consult on this proposal.

2. Original remit(s)

To appraise the clinical and cost effectiveness of cetuximab within its licensed indication in combination with platinum-based chemotherapy for metastatic and/or recurrent squamous cell carcinoma of the head and neck.

3. Current guidance

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.

4. Rationale[1]

There is no new evidence to suggest that the recommendations of TA172 should change nor any ongoing trials of cetuximab in this indication that might be expected lead to a change in the recommendations.

5. Implications for other guidance producing programmes

There is no proposed or ongoing guidance development that overlaps with this review proposal.

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[1] A list of the options for consideration, and the consequences of each option is provided in Appendix 1 at the end of this paper

6. 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 2008 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 See Appendix 2 for further details of ongoing and unpublished studies.

7. Summary of evidence and implications for review

It is unlikely that the recommendations in TA172 need to be updated because there have been no significant changes in the evidence base.

Cetuximab (Erbitux, Merck Serono) is an antibody directed at the epidermal growth factor receptor (EGFR), which has a UK marketing authorisation for the treatment of recurrent and/or metastatic squamous cell carcinoma of the head and neck (and also for locally advanced disease). This indication is unchanged from when TA172 was issued in 2009. Furthermore, the comparators in the original guidance (platinum-based chemotherapy) have stayed the same and no new comparators have emerged (docetaxel now holds a UK marketing authorisation for the treatment of head and neck cancer but this is for locally advanced disease only).

Several further papers derived from the EXTREME study have been published in the past 4 years. Some of these have published further data, showing that the addition of cetuximab to platinum-based chemotherapy did not adversely affect quality of life. (Herrero et al. 2008; Mesia et al. 2010). Others have focused on identifying a biomarker that might predict which patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck would most likely to respond to treatment with cetuximab. It has been confirmed that several candidates, including EGFR expression and EGFR gene copy number, are not suitable biomarkers so the search is continuing (Licitra et al. 2011; Vermorken et al. 2008).

Some small clinical trials have investigated novel regimens with cetuximab in combination with paclitaxel, with vinorelbine, and with carboplatin and radiotherapy, and have reported that these warrant further study (Colantonio et al. 2009; Diaz et al. 2009; Massa et al. 2010).

8. Implementation

A submission from Implementation is included in Appendix 3. Caution needs to be used when interpreting these data because they reflect total use of cetuximab, which has a UK marketing authorisation for multiple indications.

Figures 1 and 2 show that the volume and cost of cetuximab increase sharply shortly after TA172 was issued in June 2009, despite cetuximab not being recommended for treatment for recurrent and/or metastatic head and neck cancer in the NHS. This increase, however, is likely to be attributable to the publication of TA176 in August 2009, which recommended cetuximab as an option for the first-line treatment of metastatic colorectal cancer (which has a much larger patient population).

9. Equality issues

No equality issues were raised in the original guidance.

GE paper sign off: Janet Robertson, 10 May 2012

Contributors to this paper:

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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 review of the guidance should be planned into the appraisal work programme.	A review of the appraisal will be planned into the NICE's work programme.	No
The decision to review the guidance should be deferred to [specify date or trial].	NICE will reconsider whether a review is necessary at the specified date.	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
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

Options	Consequence	Selected – 'Yes/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 5 years to check whether any of the Appraisals on the static list should be flagged for review.**	**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. 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

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

iv. 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

v. 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 on improving outcomes in head and neck cancers. (CSGHN). Publication: November 2004.

Cetuximab for the treatment of locally advanced squamous cell cancer of the head and neck. TA145. Publication: June 2008. Review date: March 2011. Review decision: transfer to static list, pending publication of NCT00956007 (expected in 2015).

In progress

None

Suspended/terminated

Contusugene ladenovec within its licensed indication for the treatment of unresectable recurrent and/or refractory squamous cell carcinoma of the head and neck. Referred: March 2009. Suspended: March 2009. The manufacturer withdrew its application for a marketing authorisation.

Intensity modulated radiotherapy for head and neck cancer. Referred: March 2008. Removed from work programme: June 2009.

In topic selection[2]

[redacted]

[2] Information held by the NICE Topic Selection Team is treated as being potentially commercially sensitive by default. Details of the topics considered by NICE's Consideration Panels may be available on the NICE website, providing the manufacturers of the technologies under discussion have consented to the release of this information.

Details of changes to the indications of the technology

Indication considered in original appraisal	Proposed indication (for this appraisal)
2.1 Cetuximab is licensed for the treatment of patients with squamous cell cancer of the head and neck in combination with platinum-based chemotherapy for recurrent and/or metastatic disease.	Unchanged

Details of new products

Drug (manufacturer)	Details (phase of development, expected launch date,)
None identified	

Registered and unpublished trials

Trial name and registration number	Details
Open-label, Single-arm, Multicenter, Phase III Trial to Assess the Antitumor Activity and Safety Profile of Cetuximab in Combination With Chemotherapy for the First-line Treatment of Recurrent and/or Metastatic Squamous Cell Carcinoma of the Head and Neck in Asian Subjects CHANGE NCT01177956	Enrolment: 68 Completion date: January 2012
Cetuximab, fluorouracil (5-FU) and cisplatin alone or with docetaxel in recurrent and/or metastatic head and neck cancer CeFCiD – 1108 2008-006923-30	Enrolment: 180 Controlled, Randomised, Open label, Parallel group Status: ongoing

Appendix 3 – Implementation submission

Routine healthcare activity data

1.1 Hospital Pharmacy Audit Index (HPAI)

This section presents Hospital Pharmacy Audit Index data on the cost and volume of Cetuximab prescribed and dispensed in hospitals between July 2000 and March 2011. Caution needs to be used when interpreting these data as cetuximab has multiple indications.

Figure 1 Volume of cetuximab prescribed and dispensed in hospitals in England

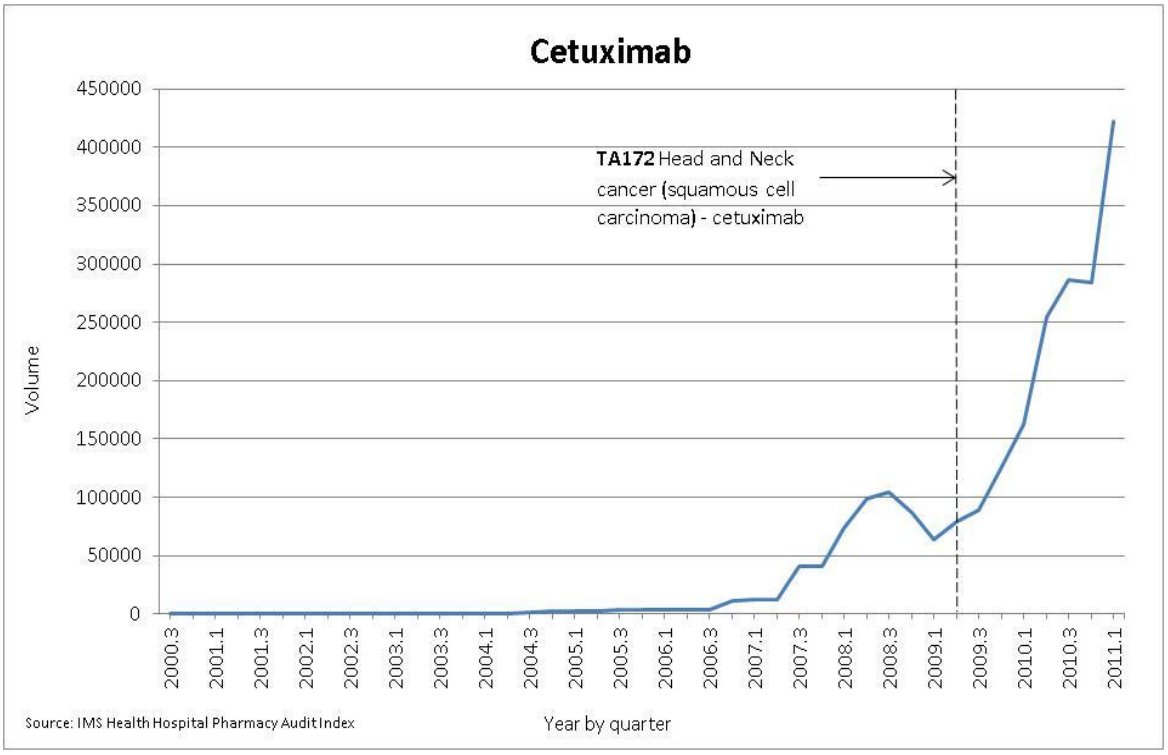
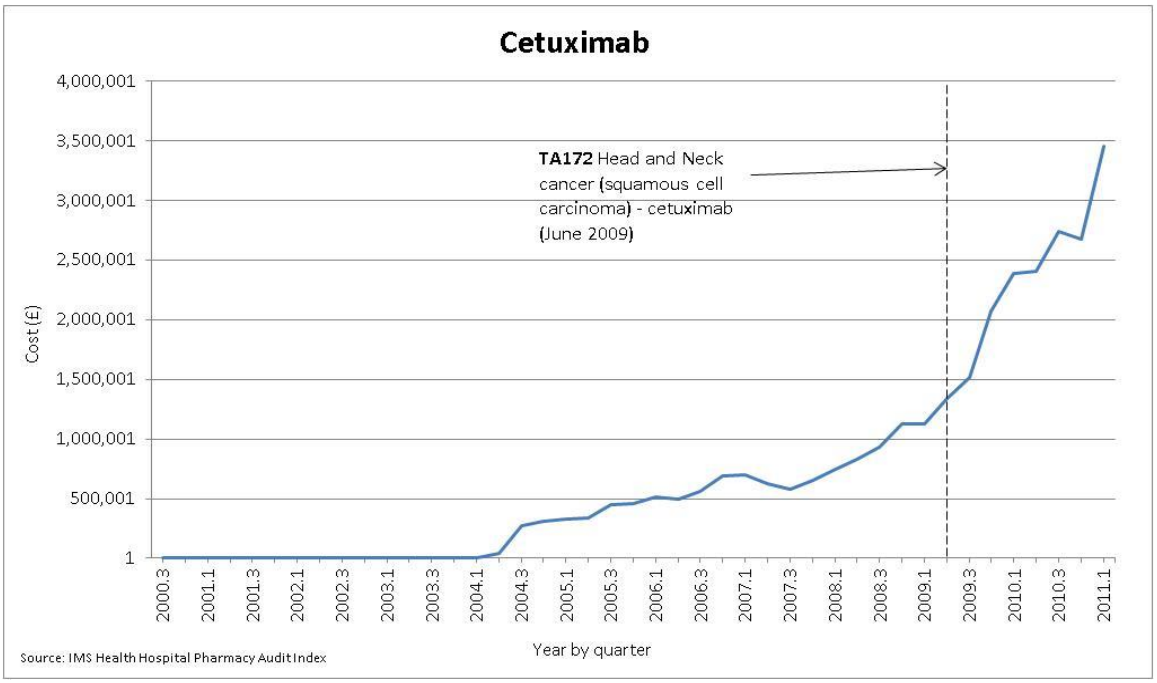


Figure 2 Net ingredient cost (£) of cetuximab prescribed and dispensed in hospitals in England



1 Implementation studies from published literature

Information is taken from the uptake database (ERNIE) website.

Nothing to add at this time.

2 Qualitative input from the field team

The implementation field team have recorded the following feedback in relation to this guidance:

Nothing to add at this time.

Healthcare activity data definitions

IMS HEALTH Hospital Pharmacy Audit Index (IMS HPAI)

IMS HEALTH collects information from pharmacies in hospital trusts in the UK. The section of this database relating to England is available for monitoring the overall usage in drugs appraised by NICE. The IMS HPAI database is based on issues of medicines recorded on hospital pharmacy systems. Issues refer to all medicines

supplied from hospital pharmacies: to wards; departments; clinics; theatres; satellite sites and to patients in outpatient clinics and on discharge.

Measures of prescribing

Volume: The HPAI database measures volume in packs and a drug may be available in different pack sizes and pack sizes can vary between medicines.

Cost: Estimated costs are also calculated by IMS using the drug tariff and other standard price lists. Many hospitals receive discounts from suppliers and this is not reflected in the estimated cost.

Costs based on the drug tariff provide a degree of standardization allowing comparisons of prescribing data from different sources to be made. The costs stated in this report do not represent the true price paid by the NHS on medicines. The estimated costs are used as a proxy for utilization and are not suitable for financial planning.

Data limitations

IMS HPAI data do not link to demographic or to diagnosis information on patients. Therefore, it cannot be used to provide prescribing information on age and sex or for prescribing of specific conditions where the same drug is licensed for more than one indication.