NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Technology Appraisals and Guidance Information Services

Static List Review (SLR)

Title and TA publication number of static topic:	**TA145; Cetuximab for the treatment of locally advanced squamous cell cancer of the head and neck**
Final decision:	The guidance will remain on the 'static guidance list'

1. Publication date:	June 2009
2. Date added to static list:	June 2011
3. Date the last searches were run:	21 February 2011
4. 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.
5. Research recommendations from original guidance:	6.1 A clinical trial on radiation therapy and cisplatin with or without cetuximab in patients with stage III or stage IV head and neck cancer (RTOG-0522) is currently recruiting patients. 6.2 The Committee recommends further research on the following: • Cetuximab in combination with radiotherapy compared with radiotherapy alone in patients with low Karnofsky performance-status scores. • Cetuximab in combination with radiotherapy compared with chemoradiotherapy in patients with high Karnofsky performance-status scores.
6. Current cost of technology/ technologies:	Intravenous infusion, cetuximab 5 mg/mL, net price 20-mL vial = £178.10, 100-mL vial = £890.50 (BNF February 2016).
7. Cost information from the TA (if available):	The acquisition cost of cetuximab is £136.50 for a 5-mg/ml, 20-ml vial (excluding VAT; 'British national formulary', edition 55). The initial dose is 400 mg/m2 body surface area. Subsequent weekly doses are 250 mg/m2 each. A course of treatment can range from 2 to 8 weeks. Assuming a body surface area range of 1.6 m2 to 1.8 m2, the drug cost of a course of treatment comprising two to eight cycles is £4778 to £5870.

8. Alternative company(ies):	None at present, though Amgen is apparently developing a biosimilar for cetuximab (Generics and Biosimilars Initiative Journal (2013) Amgen's biosimilar plans).
9. Changes to the original indication:	No change to the indication that was included in the 2011 review proposal paper.
10. New relevant trials:	Randomized Phase II/III Trial of Surgery and Postoperative Radiation Delivered With Concurrent Cisplatin Versus Docetaxel Versus Docetaxel and Cetuximab for High-Risk Squamous Cell Cancer of the Head and Neck (NCT01810913) Estimated Enrolment: 675 Estimated Primary Completion Date: May 2020 This study is ongoing, but not recruiting participants A Randomized Multicenter Phase III Study of Cisplatin Plus Radiotherapy Compared to Cetuximab Plus Radiotherapy in Locally Advanced Head and Neck Cancer (NCT01969877) Estimated Enrollment: 618 Estimated Primary Completion Date: November 2024 Randomized Phase III Study: Supplemental Parenteral Nutrition for Patients With Locally Advanced Inoperable Tumors of the Head and Neck, Receiving Definitive Radiotherapy With Cetuximab or Cisplatin (NCT02236936) Estimated Enrolment: 146 Study Start Date: April 2016 Estimated Study Completion Date: June 2019 This study is not yet open for participant recruitment. Phase III Trial of Radiotherapy Plus Cetuximab Versus Chemoradiotherapy in HPV-Associated Oropharynx Cancer (NCT01302834) Estimated Enrolment: 706 Study Start Date: June 2011 Estimated Primary Completion Date: June 2020 This study is ongoing, but not recruiting participants. Randomized Phase IV Trial to Compare Cetuximab With Concomitant Radiation

	Therapy With Concomitant Mitomycin-C and 5-Fluorouracil With Radiation Therapy for Locally Advanced Squamous Cell Carcinomas of the Head and Neck (NCT02015650) Estimated Enrolment: 70 Study Start Date: April 2014 Estimated Study Completion Date: July 2017 This study is currently recruiting participants. TROG12.01 A Randomised Trial of Weekly Cetuximab and Radiation Versus Weekly Cisplatin and Radiation in Good Prognosis Locoregionally Advanced HPV-Associated Oropharyngeal Squamous Cell Carcinoma (NCT01855451) Estimated Enrolment: 200 Study Start Date: June 2013 Estimated Study Completion Date: June 2021 This study is currently recruiting participants. Determination of Epidermal Growth Factor Receptor-inhibitor (Cetuximab) Versus Standard Chemotherapy (Cisplatin) Early And Late Toxicity Events in Human Papillomavirus-positive Oropharyngeal Squamous Cell Carcinoma (NCT01874171) Estimated Enrollment: 304 Study Start Date: October 2012 Estimated Study Completion Date: September 2019 This study is currently recruiting participants.
11. Relevant NICE guidance (published or in progress):	NICE care pathway Head and neck cancer NICE care pathway Upper aerodigestive tract cancer NICE guidance in development [GID-QS10018] Head and neck cancer Anticipated publication date: February 2017. NICE guidance in development [GID-TA10058] Head and neck cancer (squamous cell carcinoma) - cetuximab (review of TA172) [ID1016] - CDF rapid reconsideration process. Anticipated publication date: February 2017.
12. Relevant safety issues:	Nothing relevant.

13. Any other additional relevant information or comments:	Radiation Therapy With or Without Cetuximab in Treating Patients Who Have Undergone Surgery for Locally Advanced Head and Neck Cancer (NCT00956007) Estimated Enrolment: 700 Study Start Date: November 2009 Estimated Primary Completion Date: August 2021 This study is currently recruiting participants.
14. Technical Lead comments and recommendation:	Since NICE technology appraisal guidance 145 was moved to the static guidance list in 2011, the marketing authorisation for cetuximab has not changed. Additionally no relevant safety issues have been identified, or has NICE published any new guidance appraising technologies for treating locally advanced squamous cell cancer of the head and neck. NICE technology appraisal guidance recommends cetuximab for specific people with locally advanced squamous cell cancer of the head and neck: Karnofsky performance-status score is 90% or greater and for whom all forms of platinum-based chemoradiotherapy treatment are contraindicated. When it was recommended that NICE technology appraisal guidance 145 should be moved to the 'static guidance list', it was on the condition that the decision to review the guidance should be deferred until after 2015 when the results of NCT00956007 became available. This study includes people with Zubrod performance status 0–1 (equivalent to a Karnofsky performance-status score of 80-100), and is comparing radiation therapy with or without cetuximab in people with locally advanced head and neck cancer. However, NCT00956007 is still recruiting participants and the estimated primary completion date is now August 2021. During the original appraisal, the committee was also not presented with any evidence comparing cetuximab plus radiotherapy with chemoradiotherapy on which an estimate

	of the clinical and cost effectiveness could be based. Therefore the committee was unable to make any recommendations on its use as an alternative to chemoradiotherapy. Several ongoing trials may provide evidence that could enable the clinical and cost effectiveness of cetuximab plus radiotherapy compared with chemoradiotherapy to be inferred. In particular, NCT01969877, but this is not due to report until November 2024. The list price of cetuximab for a 5mg/mL, 20-mL vial has increased from £136.50 to £178.10. However, it is unlikely that this change in price would increase the ICER beyond a level that is normally considered to be a cost-effective use of NHS resources for the specific populations NICE has recommended cetuximab. It should also be acknowledged that a biosimilar for cetuximab is currently under development. Overall, no new evidence has been identified that would impact the current recommendations in NICE technology appraisal guidance 145. It is therefore appropriate for the guidance to remain on the 'static guidance list'.

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Date of IS searching: 26/02 – 03/05 2016

Appendix 1 – explanation of options

Options	Consequence	Selected – 'Yes/No'
The guidance will remain on 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
The decision to review the guidance will be deferred to specify date or trial	NICE will consider whether a review is necessary at the specified date. NICE will actively monitor the evidence available to ascertain when a consideration of a review is more suitable.	No
A full consideration of a review will be carried out through the Review Proposal Process	There is evidence that could warrant a review of the guidance. NICE will schedule a consideration of a review, including a consultation with relevant consultees and commentators.	No
The guidance will be withdrawn	The guidance is no longer relevant and an update of the existing recommendations would not add value to the NHS. NICE will schedule a consideration of a review, including a consultation with relevant consultees and commentators.	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	No

	withdrawn. NICE will schedule a consideration of a review, including a consultation with relevant consultees and commentators.	