NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Consideration of consultation responses on review proposal

Review of TA 118 Colorectal cancer (metastatic) - bevacizumab & cetuximab - This guidance was issued in January 2007 with a review date of May 2009.

Background

At the GE meeting on 25 August 2009 it was agreed the review plans for this guidance would be consulted on. A four-week consultation was conducted with consultees and commentators. The responses are presented below.

Proposal put to consultees:	1. An appraisal to update part of TA 118 covering bevacizumab, cetuximab and (additionally) panitumumab for the treatment of metastatic colorectal cancer following the failure of first line chemotherapies. This update would also include the terminated appraisal TA150 Cetuximab for the treatment of metastatic colorectal cancer following failure of oxaliplatin-containing chemotherapy. 2. The remaining guidance in TA118 covering bevacizumab plus irinotecan for first line treatment of metastatic colorectal cancer will be considered for review together with other first line treatment appraisals of metastatic colorectal cancer. That we consult on this proposal.

GE is asked to consider the original proposal in the light of the comments received from consultees and commentators, together with any responses from the appraisal team. It is asked to agree on the final course of action for the review.

Recommendation post consultation:	1. An appraisal to update part of TA118 is carried out covering bevacizumab, cetuximab and (additionally) panitumumab for the treatment of metastatic colorectal cancer following the failure of first line chemotherapies. This update will also include the terminated appraisal TA150 Cetuximab for the treatment of metastatic colorectal cancer following failure of oxaliplatin-containing chemotherapy. This appraisal of second and subsequent line treatments, includes a number of licence extensions that have been granted but have not been referred to NICE so remits for these extensions will be sought from the Department of Health before the appraisal will begin.

	2. A separate appraisal of the remaining recommendations in TA118 (bevacizumab plus irinotecan for first line treatment of metastatic colorectal cancer) is carried out (subject to a patient access scheme being referred to NICE for consideration by the Department of Health).

Respondent	Response to proposal	Details	Comment from Technology Appraisal
Amgen	Agree	In response to the question regarding timelines around on-going research which might affect the scheduling of this review should it proceed, we would like to inform the Institute of a recently completed study of panitumumab in combination with FOLFIRI compared to FOLFIRI alone as second line therapy for metastatic colorectal cancer (NCT00339183). [redacted]. This study evaluates panitumumab as second line treatment following failure of first-line chemotherapy. The population studied in the panitumumab trial is different from the second line treatment populations studied in the cetuximab trial in terms of inclusion and exclusion criteria around first-line chemotherapy regimens, and the treatments used in second line (panitumumab was evaluated in combination with FOLFIRI whereas cetuximab was evaluated in combination with irinotecan).	Comment noted. An appraisal of panitumumab in combination with chemotherapy was referred to NICE in March 2009 as part of the 20th wave. In order to provide timely guidance to the NHS this indication is being considered in a separate appraisal.
Amgen	Agree	We would like to seek clarification on the indications that would be considered after failure of first line treatment for cetuximab in this proposed review. Reference is made to the indications for cetuximab after the failure of first-line therapy on Page 5, *"However, the indications for treatment after the failure of first line chemotherapy in TA118 (combination with irinotecan), TA150 (combination with oxaliplatin) and the monotherapy indication may be considered together as reflecting the available options for adding cetuximab to standard treatment."* We would appreciate clarification from the Institute that TA 150 evaluated cetuximab in combination with irinotecan after failure of oxaliplatin-containing therapy instead of cetuximab in	Comment noted. You are correct; TA150 is a terminated appraisal of cetuximab in combination with irinotecan (not oxaliplatin as is mistakenly stated in the review proposal) after the failure of oxaliplatin containing chemotherapy.

		combination with oxaliplatin as stated above.	
Amgen	Agree	We would like to provide clarification on the monotherapy indication for panitumumab after failure of other chemotherapy regimens. The Institute make a reference on Page 5 which seems to suggest that Vectibix monotherapy is indicated for the same population as Erbitux monotherapy, *"However, as this treatment is indicated for the same population as cetuximab, for a similar point in the care pathway it would be appropriate to combine this indication with any appraisal of cetuximab for treatment subsequent to first line therapy."* Panitumumab monotherapy is not entirely indicated for the same population as cetuximab monotherapy as 100% of patients in the panitumumab trial received two lines of prior chemotherapy compared to around 20% in the cetuximab trial. Therefore, it appears that panitumumab was studied in a patient population that had failed more, i.e. at least two, prior therapies compared to the cetuximab patient population.	Comment noted. The review will appraise cetuximab and panitumumab in accordance with their marketing authorisations. Differences in the clinical trial populations would be considered as part of the assessment and appraisal processes.
Amgen	Agree	We would appreciate more clarification on the timing of the review especially with regards the timing of the proposed initiation of the review and the anticipated deadline for manufacturers to make their submissions to this review. The proposal states that the scoping work would start in October 2009 and that the Appraisal Committee would consider the appraisal in November 2010 with expected publication in March 2011. We would like to request that the Institute consider extending the deadline for manufacturer submission, as we were excluded from the initial email sent by the Institute to the various stakeholders when the review process began in August 2009, and require sufficient time to prepare for the review. We were only informed of the possibility of this appraisal at least two months later than other stakeholders.	Comment noted. Timelines will be set if the decision to update is made and once the required referral has been received. These will be provided when the update has been scheduled into the work programme.
Association of Cancer Physicians	Agree	-	Comment noted.

Merck Serono	Disagree with first proposal	The scope for this appraisal should be focussed on a review of TA 118 and the recent addition of monotherapy to the cetuximab license in metastatic colorectal cancer. This would mean a review of cetuximab in combination with chemotherapy or as a monotherapy in patients with metastatic colorectal cancer who have failed two previous chemotherapeutic regimes in the metastatic setting.	Comment noted. NICE can provide maximum value to the NHS by considering all relevant technologies used at the same point in the treatment pathway (with consideration paid to timely production of guidance). In the context of reviewing TA118, this would include panitumumab, cetuximab and bevacizumab in accordance with their marketing authorisations.
	Agree to second proposal	To updating the remaining guidance on bevacizumab plus irinotecan for first line treatment of metastatic colorectal cancer is deferred and it is considered for review with other first line treatment appraisals of metastatic colorectal cancer.	Comment noted. A review of the guidance on bevacizumab has been recommended. See comment and response to the manufacturer of bevacizumab (conditional on the patient access scheme being referred to NICE for consideration).
National Cancer Research Institute	Agree	-	Comment noted.
National Collaborating Centre for Cancer	Agree	-	Comment noted.
NHS Quality Improvement Scotland	Disagree	Has no evidence to present which would make an early review beneficial.	The marketing authorisations for the technologies under consideration have changed and therefore it is appropriate that NICE considers a review of its guidance.

Pfizer	No comment	-	Comment noted.
Royal College of Nursing	No comment	-	Comment noted.
Royal College of Physicians, Medical Oncology Joint Special Committee	Agree	-	Comment noted.
Royal College of Radiologists	Agree	-	Comment noted.
Research Institute for the Care of Older People	No comment	-	Comment noted.
Roche	Disagree	Bevacizumab be included in the reappraisal going forwards without the decision being deferred. This is because we would like to make a re-submission with an accompanying Patient Access Scheme which would mean that potentially the combination of bevacizumab with irinotecan will now be judged as a cost effective use of NHS resources and within the cost effectiveness thresholds normally applied by Appraisal Committees.	Comment noted. It has been agreed that the guidance on bevacizumab plus irinotecan be reviewed (conditional on the patient access scheme being referred to NICE for consideration). The proposal has been amended accordingly.
SanofiAventis	No comment	-	Comment noted.

No response received from the following consultees and commentators:

Patient/carer groups	Professional groups	Possible comparator manufacturer(s)
• Afiya Trust	• Association of Coloproctologists of Great Britain	• Actavis UK (oxaliplatin)

• Beating Bowel Cancer • Black Health Agency • Bowel Cancer UK • CANCERactive • Cancer Black Care • Cancer Equality • Chinese National Healthy Living Centre • Colostomy Association • Confederation of Indian Organisations • CORE - The Digestive Disorders Foundation • Counsel and Care • Equalities National Council • Helen Rollason Heal Cancer Charity • Ia: Ileostomy and Internal Pouch Support Group • Lynn's Bowel Cancer Campaign • Macmillan Cancer Support • Maggie's Centres • Marie Curie Cancer Care • Muslim Council of Great Britain • Muslim Health Network • National Cancer Alliance • National Council for Palliative Care • Ostomy Lifestyle Centre • Pelican Cancer Foundation • South Asian Health Foundation • Specialised Healthcare Alliance • Sue Ryder Care • Teenage Cancer Trust • Tenovus Cancer Information Centre	• Association of Surgeons of Great Britain and Ireland • British Association for Services to the Elderly • British Association of Surgical Oncology • British Geriatrics Society • British Oncological Association • British Psychosocial Oncology Society • British Society of Gastroenterology • Cancer Network Pharmacists Forum • Cancer Research UK • Royal College of Anaesthetists • Royal College of General Practitioners • Royal College of Pathologists • Royal College of Surgeons • Royal Pharmaceutical Society • Royal Society of Medicine – Intellectual Disabilities Forum • United Kingdom Clinical Pharmacy Association • United Kingdom Oncology Nursing <u>General</u> • Board of Community Health Councils in Wales • British National Formulary • Department of Health, Social Services and Public Safety for Northern Ireland • Medicines and Healthcare products Regulatory Agency • National Association of Primary Care • National Public Health Service for Wales • NHS Alliance • NHS Confederation • NHS Purchasing and Supply Agency • Scottish Medicines Consortium	• Amgen (panitumumab) • Hospira UK (oxaliplatin, fluorouracil and calcium levofolinate) • Medac UK (oxaliplatin and fluorouracil) • Merck Serono (tegafur uracil) • Roche Products (capecitabine) • Wyeth Pharmaceuticals (calcium levofolinate) <u>Relevant research groups</u> • Bowel & Cancer Research • Institute of Cancer Research • MRC Clinical Trials Unit • National Cancer Research Network • National Institute for Health Research • Policy Research Institute on Ageing and Ethnicity <u>Assessment Group</u> • National Institute for Health Research Health Technology Assessment Programme <u>Associated Public Health Groups</u> • none

GE paper sign-off:

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