This statement was provided after the Committee meeting. NICE has requested this statement so that consultees or commentators not present at the Committee meeting can see a written record of the clinical specialist's opinion.

Cetuximab (mono- or combination chemotherapy), bevacizumab (combination with non-oxaliplatin chemotherapy) and panitumumab (monotherapy) for the treatment of metastatic colorectal cancer after first-line chemotherapy

1 There is good evidence for the efficacy of cetuximab monotherapy in improving survival as second or third line therapy in advanced colorectal cancer, which has emerged from the Karapetis study. This is an important advance in the treatment of colon cancer and is widely accepted by oncologists in the UK as a treatment option which should be made available. However there is no clear data provided by Merck-Serono as to median duration of treatment for these patients which would allow accurate estimation of QALYs

2 Emerging evidence from several studies suggests a survival advantage from combination of cetuximab with irinotecan. A survival advantage for this regimen over cetuximab alone was found with the BOND study. More recent data has not been included with the submission including the CRYSTAL study. Despite the fact that this was a first line trial there is no reason to suppose that these results would not be replicated in the second line setting. Most oncologists in the UK would favour the option of including a cetuximab/irinotecan combination in the second line (wild type KRAS) after progression on an oxaliplatin containing regimen.

3 The evidence for the impact of treatment with panitiumumab on overall survival is less marked, due to the extensive (and justified) crossover in the pivotal study by van Cutsem. Therefore complex assumptions have been made to assess benefit, such as grouping mutant KRAS expressing patients with the control group despite their participation in crossover. However this study does seem comparable in impact with the cetuximab monotherapy data and most oncologists would wish to have availability of the agent. There is no discussion regarding combination of this agent with chemotherapy.

4 The most compelling evidence for efficacy of bevacizumab is its use in combination with irinotecan and fluorouracil. Even though the regimen used in the Hurwitz study, which demonstrated significant effects on survival, is different from the FOLFIRI regimen common in the UK, there is no reason to postulate that this would impact on the beneficial effect of bevacizumab. The use of this combination has been rejected by NICE primarily due to the differences in the regimen, although the majority of oncologists would accept the benefits of this combination and would favour its availability in this setting. In view of the recent decision by

NICE rejecting the combination of bevacizumab with oxaliplatin regimens, no application has been made for this.

Professor Daniel Hochhauser, UCL Cancer Institute 7th August 2011