NICE National Institute for Health and Care Excellence

10 Spring Gardens
London
SW1A 2BU
United Kingdom

+44 (0)845 003 7780

Sent by email

Dr Charlie Nicholls
Head of Health Outcomes
Sanofi
One Onslow Street
Guildford
Surrey
GU1 4YS

13 December 2013

Dear [redacted]

Appeal against the FAD for aflibercept for the treatment of metastatic colorectal cancer

Thank you for your letter dated 6 December 2013. This letter represents my final decision on initial scrutiny.

1.1. In concluding that aflibercept "did not meet the criteria for an end of life therapy as defined by NICE" the Appraisal Committee has incorrectly applied the Supplementary Advice issued by the Institute.

I have carefully considered the points you make. However I remain unable to read the Supplementary Advice as you suggest. It seems inescapable to me that the requirement set out in paragraph 2.3.1 that estimates of extension to life be robust (and assumptions plausible etc) applies when and not after deciding whether the criterion described in 2.1.2 is satisfied. I do not think that the use of "in addition" in paragraph 2.3 implies that paragraph 2.3 is a standalone criterion applied after paragraphs 2.1 and 2.2, rather than an instruction as to the approach to take in paragraph 2.1.

I note your point that it is important to know if a product falls within the EoL criteria even if paragraph 2.3 then applies. I would reply that it is important to know if the supplementary advice has been applied, and if not why not. In any case on my understanding of the Advice it is not possible to say the product is within the EoL criteria at all if the estimates are not robust. I understand that there is a difference between the case where the estimates are robust and are not within the criteria, and the case where the estimates are not robust but the true values could be within the criteria, but I do not believe that NICE's processes, or fairness, require any more than that guidance should be clear which of those two possibilities applies.

I note that you consider that the Committee is wrong as to whether the estimates were in fact robust, but that is going to be considered under ground two. Finally on

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this point, I appreciate that this argument has not previously been considered by an Appeal Committee, but do not feel that means I should allow it to proceed where I have concluded that it cannot possibly succeed.

My conclusion is that this is not a valid appeal point.

1.2. The Appraisal Committee's conclusions with respect to the appropriate time horizon for this appraisal are unclear and relevant evidence appears to have been disregarded

Having considered the points you make I now agree that this is a valid appeal point. This seems to me to duplicate point 1.4 below as the evidence said to be disregarded is the same. I will refer the point to an appeal panel as one combined point "did the committee have regard to all of the evidence on patient survival".

1.3. The Appraisal Committee's conclusion that the true mean overall survival benefit is likely to be closer to the median survival of 1.44 months, rather than Sanofi's extrapolation of 4.7 months is unexplained and the basis for the Committee's view is unclear

Accepted as valid.

1.4. The Appraisal Committee has seemingly disregarded evidence indicating that improved survival in patients with metastatic colo-rectal carcinoma may be attributed to improved medical management as well as resection of metastases

This point seems to me to duplicate point 1.2 above, as the evidence said to be disregarded is the same. I will refer the point to an appeal panel as one combined point: "did the committee have regard to all of the evidence on patient survival".

2.1 The Appraisal Committee have incorrectly assumed that further follow up data from the VELOUR trial are available and this has influenced their conclusions in this appraisal.

and

2.2 The Committee's conclusion that the data relating to abflibercept were not sufficiently robust to accept that a three month life extension benefit was produced is inconsistent with the available evidence and therefore unreasonable.

Accepted as valid.

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2.3 The Appraisal Committee has provided no explanation for the inconsistencies in its approach to the assessment of the overall survival benefit associated with aflibercept in this appraisal and that for panitumumab in TAG 242: in the absence of an explanation, these inconsistencies suggest an arbitrary approach which is unreasonable.

While my reservations remain, on balance I now agree that it is appropriate for the Appeal Committee to consider what if any were the requirements of consistency in this appraisal.

A valid ground two appeal point.

2.4 The Committee's rejection of utility data from the mCRC study in favour of an arbitrary estimate for progressed disease is unreasonable.

Withdrawal of appeal point noted.

This is the final decision on initial scrutiny. The valid appeal points are [1.2 combined with 1.4] 1.3, 2.1, 2.2, and 2.3.

Yours sincerely

[redacted]
Appeals Committee Chair
National Institute for Health and Care Excellence