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18 February 2015

Dear [redacted]

Final Appraisal Determination: Topotecan, pegylated liposomal doxorubicin hydrochloride, paclitaxel, trabectedin and gemcitabine for treating recurrent ovarian cancer (including reviews of technology appraisal guidance 91 and 222)

Thank you for your letter of 11 February 2015. This letter is my final decision on initial scrutiny.

Ground 1(a)

1.1 Exclusion of the appraisal committee of relevant covariates in the adjusted analysis of trabectdin is unjustified.

I have considered whether this could be a valid ground 1(a) or a ground 2 point. My view on whether this can be a valid ground 1(a) point remains as set out in the initial scrutiny letter.

So far as considering this as a ground 2 point, I refer again to the appeal panel's decision in aflibercept, which concluded that "*Therefore for guidance to be unreasonable on the grounds of inconsistency the Panel feels the inconsistency needs to be very clear indeed*." I do not consider this to be arguable given the explanation in the FAD and the different comparisons and analysis required by the STA and MTA processes.

I have concluded that this is not a valid appeal point.

1.2 Different interpretation of the evidence by the same appraisal committee for the MTA and TA222 regarding the use of head to head data for trabectedin to address the decision problem for the non-platinum network is irrational and unfair

I have considered whether this could be a valid ground 1(a) or a ground 2 point. My view on ground 1(a) remains as set out in the initial scrutiny letter.

On ground 2, I note that this point has been addressed at paragraph 4.3.16 onwards of the FAD. Furthermore, an MTA may require a different analysis compared to an STA, given the greater number of comparisons that need to be made.

I have concluded that this is not a valid appeal point.

Ground 2

2.1 The appraisal committee's rationale for not using adjusted clinical effectiveness results for the cost effectiveness evaluation of trabectedin in the MTA is flawed and inconsistent with the previous TA222 appraisal and NICE DSU guidance

I have considered whether this could be a valid ground 1(a) or a ground 1(b) point.

I repeat my comments above and in my previous letter. Again, TA222 was a separate appraisal and as an STA was answering a different decision problem to this MTA, which involves the appraisal of the relative cost effectiveness of several treatments. The ERG report informing a particular appraisal does not amount to guidance that must be followed in subsequent appraisals, as your argument suggests.

On your procedural fairness argument, I do not consider that Pharma Mar could have a reasonable expectation that the analysis in this appraisal would be carried out in a particular way. It has been long established in decisions of the appeal panel that the outcome of one appraisal does not bind decision-making in another appraisal.

I have concluded that this is not a valid appeal point.

2.2 The Appraisal Committee failed to take into account key differences in baseline characteristics and trial design of relevant studies that have informed the clinical and cost-effectiveness results and subsequent recommendations for the FAD including that of trabectedin.

Thank you for the additional information you have provided on this point. I refer to my previous letter regarding your complaint regarding the failure to take into account key differences in baseline characteristics. This is not a valid appeal point.

However, the issues you raise about the conduct of sensitivity analyses in accordance with paragraph 5.2.14 of the Institute's Guide to the Methods of Technology Appraisal is a valid ground 1(a) point.

2.3 the different interpretation of the evidence by the same appraisal committee for the MTA and TA222 regarding the use of direct head to head data for trabectedin to address the decision problem for the non-platinum network is irrational and unfair.

I have considered whether this could be a valid ground 1(a) or a ground 2 point. For the reasons outlined above and in my previous letter, this is not a valid appeal point.

2.6 Recommendations for use of off-label PLDH in combination with platinum are unlawful.

Thank you for providing further details about your concerns. I note that footnote 2 to paragraph 1.3 of the FAD explains that *"NICE received a remit to appraise this combination* [PLDH in combination with platinum] *under Regulation 5 of the National Institute for Health & Care Excellence (Constitution & Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013*". I repeat that NICE's appeal process cannot come to a ruling on what the Department of Health is or is not legally able to do. That is a matter to be raised with the Department of Health.

However, concerns about the process by which this extension in remit was dealt with by the Committee and how this impacted on consultees and commentators can be raised as a valid appeal point. Therefore this ground will proceed to the appeal. The appeal panel will consider which ground it is most appropriate to consider your concerns under once it has considered the arguments in full.

I can therefore confirm the valid appeal points as: 2.2 (to be dealt with under ground 1(a)), 2.4, 2.5 and 2.6.

Yours sincerely

[redacted]

[redacted]

National Institute for Health and Care Excellence