

We would strongly agree with section 4.6 as the primary outcome of the pivotal trial was not significant:

The Committee also noted that the difference in overall survival between the study arms was not statistically significant for the ITT population, but was significant for the eligible ITT population. The Committee was aware that the difference between the two analyses resulted from the exclusion of 13 patients from the eligible ITT analysis. A greater proportion of ineligible patients came from the best supportive care arm than from the vinflunine arm (8% versus 2%) and this lowered the overall survival in the best supportive care arm in the eligible ITT analysis. The Committee considered that the results from the ITT population were the most appropriate basis for its deliberations because randomisation had not been broken and therefore the trial reflected what is likely to happen in clinical practice. It also noted that there were no significant differences in health-related quality of life between patients receiving vinflunine and those receiving best supportive care alone. The Committee concluded that the clinical effectiveness of vinflunine compared with best supportive care had not been conclusively demonstrated because of the uncertainty in the overall survival results

We would also endorse the comments in 4.11:

The Committee discussed the inclusion of adverse events in the model and noted that although the costs of adverse events were included, the disutility associated with them was not. It discussed the cost of grade 3 and 4 constipation and considered that it was likely to be significantly higher than that used in the model (£39).

We believe that the treatment costs for adverse effects to be higher than that estimated – not just for constipation – but also for neutropenia, as it would appear that the HRG used to estimate the neutropenia costs does not take into account the excluded drug costs for the management of febrile neutropenia.

Finally we would also query the acceptance that the number of people likely to require second line therapy as estimated by the manufacturer (1500) is a small population (as per NICE end of life criteria). Nationally about 10,000 patients a year are diagnosed with this form of cancer (according to Horizon Scanning centre) with c.4000 deaths. It's likely therefore that more than 1500 cited by the manufacturer and this would need further clarification.