YONDELIS® (TRABECTEDIN) FOR THE TREATMENT OF SOFT TISSUE SARCOMA

RESPONSE TO ACD REPORT ON COST-EFFECTIVENESS OF TRABECTEDIN

14th JULY 2009

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PharmaMar believe that the ERG critique of the cost-effectiveness model was largely fair and balanced. However, a thorough review of the ACD document identified two statements which appear to be inconsistent with the evidence presented. These issues are detailed below.

1. On page 11 (section 3.19, first bullet), the ACD states that a key uncertainty in the cost-effectiveness estimates is that **"It is unclear how the estimated ICER would relate to patients with types of soft tissue sarcoma other than L-sarcomas, because the STS-201 trial included only participants with L-sarcomas."**

This uncertainty has been addressed in the sensitivity analysis. The manufacturers' submission included a sensitivity analysis using pooled data from three non-comparative Phase II trabectedin trials. This pooled dataset included patients with other non L-sarcoma histology types. This sensitivity analysis reported a cost per QALY of £50,017 (£55,377 with the utility adjustment in the best supportive care arm). This analysis is representative of a population of soft tissue sarcoma patients including some who do not have L-sarcomas. The ERG received and discussed this analysis. We contend that this issue has been addressed in the evidence presented, that the cost-effectiveness of trabectedin in a wider population of soft tissue sarcoma patients has been explored, and that cost-effectiveness in the wider patient populations has been found to be similar to that in L-sarcomas, within the limits of the evidence available.

2. In light of the comments made by the clinical specialists and patient group experts, PharmaMar accept that the choice of utilities from non-small cell lung cancer does not fully reflect utility in soft tissue sarcoma. The large decline in patient utility between the progression free state and the progressed health state may not be reflective of the changes in quality of life expected for soft tissue sarcoma.

On page 16 (section 4.10), the ACD states **"Conversely, it [the committee] heard that if these differences were modelled as a longer period of higher utility followed by rapid decline at the end of life, this could be expected to increase the ICER".** In a revised version of the model consistent

with other ERG comments, an additional model scenario was run to explore rapid decline in utility at the end of life. In this analysis a utility of 0.653 was applied to all health states in the model and a utility decrement of -0.18 is applied to the month before death. This structure more accurately reflects the description provided by the clinical specialists and patient group. In this analysis, the ICER falls from £61,064 to £51,000 per QALY. This finding is supported by additional utility analysis undertaken by the ERG (see page 50 of the ERG report) in which the utilities were set to 0.7 in progression free and 0.6 in progressed. This analysis reduced the ICER to £50,297. We contend that this statement is not correct and this sentence should be deleted and replaced with the words;

In a scenario where utility was modelled as a longer period of higher utility followed by rapid decline at the end of life, the ICER would decrease to around £51,000 per QALY gained.